Specialty Natural Rubber Products for Biomedical Applications

Dissertation

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Abstract

Rubber medical devices are essential in the prevention of healthcare-associated infections (HAIs). Although natural rubber has been demonstrated to have superior physical qualities compared to synthetic rubber, the emergence of widespread latex allergies in the 1980s and 1990s caused the demand for natural products to sharply decline. In recent years, a woody shrub known as guayule (*Parthenium argentatum*) has been studied as an alternative source of natural rubber to the traditional rubber tree (*Hevea brasiliensis*). Guayule latex naturally does not contain the soluble protein levels required to induce a Type I latex allergy, unlike *Hevea* latex. It is also softer, stronger, and stretchier than *Hevea*, making it ideal for biomedical devices. In this research, prototype guayule latex medical products were developed and tested alongside products available on the market. An automated glove durability assessment device was constructed to objectively determine glove performance in wet and dry environments, allowing the user to rank gloves in terms of durability. The prototype guayule latex gloves were found to have superior durability in these tests as well as others, providing evidence of the superiority of guayule latex as a biomaterial. Gloves that underperformed in durability tests underwent a series of material identification tests, including Fourier Transform Infrared and Nuclear Magnetic Resonance testing, which identified Vglove brand gloves as being composed mostly or completely of polyvinylchloride (PVC), not pure nitrile as

advertised. In addition, a hypoallergenic xanthate-based accelerant system used to vulcanize guayule latex was optimized to create an endotracheal tube balloon cuff with high tensile strength and low Young's Modulus. This guayule cuff had a much lower leakage rate than the traditional PVC cuff. Overall, high-quality rubber medical devices, such as those made from guayule, preserve the safety of healthcare workers and patients, and can prevent hundreds of HAI deaths each year.

Dedication

Dedicated to Anna, Bob, Lexi, and Matthew for all their love and support.

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Publications

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Herkins, A., & Cornish, K. (2023). Durability variation among medical gloves made from existing and new elastomers poses a risk to public health. Global Challenges, 7(9). https://doi.org/10.1002/gch2.202300100 (Peer Reviewed)

Herkins, A., Dey, S., Conroy, D., & Cornish, K. (2024). Nitrile Glove Composition and Performance – Substandard Properties and Inaccurate Packaging Information. PLOS One. Under Review. (Peer Reviewed)

Herkins, A., & Cornish, K. (2024). Medical Glove Durability is Differentially Affected by Solvent Exposure Impacting User Safety. Patient Safety in Surgery. Under Review. (Peer Reviewed)

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Wilson, T. G., Venturini, A. N., & Christy, A. D. (2021, July), Student Opinion on Teaching Thermodynamics Through Synchronous and Asynchronous Distance Learning Paper presented at 2021 ASEE Virtual Annual Conference Content Access, Virtual Conference. https://peer.asee.org/37748 (Peer Reviewed)

Fields of Study

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Chapter 1. Introduction

With over 400 applications in medical devices, natural rubber (NR) is a vital biomaterial in the medical field (Mooibroek & Cornish, 2000). Common devices include membranes, diaphragms, blood pressure cuff coils, seals, covers, tubes, gloves, condoms, balloons, and baby bottles, among others (Rahimi & Mashak, 2013). In recent years, NR has also been used in tissue engineering, tissue repair, and controlled drug delivery systems due to its biocompatibility (Guerra et al., 2021).

The first recorded use of rubber medical gloves was in 1889 when scrub nurse Caroline Hampton Halsted requested them from her husband William Stewart Halsted as a solution to her severe contact dermatitis from handling chemical disinfectants (Lathan, 2010). Doctors later realized that infection rates were greatly reduced, some by nearly 100%, when rubber gloves were worn during surgeries, and the use of medical gloves became more widespread (Lathan, 2010). Today, rubber gloves are a standard piece of personal protective equipment (PPE) worn by medical professionals worldwide to prevent the spread of disease.

Unfortunately, there are several issues with NR medical device production and regulation. For instance, most NR medical devices are produced with latex (NRL) tapped from the Brazilian rubber tree, *Hevea brasiliensis*. If *Hevea* latex products are not properly leached during manufacture, they contain enough soluble protein content to

induce a Type I hypersensitivity allergy. Sensitized people can then react to miniscule amounts of proteins in NRL or NR products, which can lead to anaphylactic shock and even death (Cornish, 2012). Although NR products are stronger, softer, and stretchier than synthetics, the threat of latex allergies caused demand to shift from products made from NR to petroleum-derived synthetics (Abraham & Ramesh, 2002). As a result, synthetic medical products, such as endotracheal tube balloon cuffs made from polyvinyl chloride (PVC), do not have the necessary material properties to consistently function as intended, leading to adverse patient outcomes.

The lax regulation of NR medical devices is also a concern. ASTM International, an organization that publishes standards for hundreds of devices, does not currently have a standard for medical glove durability once the gloves have been removed from their packaging by the consumer. The current standards only include the required mechanical properties of unaged and aged gloves before they are packed and shipped (ASTM International 2019a, 2019b), and one that simply tests for existing holes - a simple water inflation test in which a glove is placed on a mandrel, filled with tap water, and visually inspected for leaks (ASTM International 2019c). The United States Food and Drug Administration (FDA) inspection rate is extremely low due to lack of inspectors and sheer volume of imported products. In addition, the only penalty for manufactures found to market gloves below the mandated standards is a minor fine, which does not deter these manufacturers from continuing to produce substandard products.

The objectives of this research are to 1) develop a device to objectively determine glove durability and implement it as part of a new ASTM International standard for glove

durability, 2) identify which glove manufacturers are producing substandard gloves and determine the causes of this underperformance including through material identification tests, and 3) develop and test guayule latex medical gloves and endotracheal tube balloon cuffs as circumallergenic (avoids all allergies) alternatives to *Hevea* and synthetic rubber products.

Chapter 2. Literature Review

2.1 Rubber Polymers

2.1.1. Natural Rubber

Natural rubber (*cis*-1,4-polyisoprene) (NR) is a plant-produced polymer essential in the manufacture of over 50,000 products, 400 of which are medical devices (Mooibroek & Cornish, 2000; Nair, 2021). Nearly all NR is tapped from the Para (or Brazilian) rubber tree (*Hevea brasiliensis*), a species native to the Amazon basin but now cultivated primarily in Southeast Asia (Mooibroek & Cornish, 2000). These trees produce a milky white substance called latex (NRL), which is a colloidal suspension of membrane bound rubber particles in aqueous solution (Mooibroek & Cornish, 2000). When rubber trees are tapped, an incision is made in the trunk of the tree, allowing the latex to dribble out and be collected in small cups.

Although 2,500 rubber-producing plant species are known, only three species are in commercial development: the Para rubber tree, the rubber dandelion (*Taraxacum kok-saghyz*), and the woody shrub guayule (*Parthenium argentatum*) (Venkatachalam et al., 2013). Both the rubber dandelion and guayule have shown potential as alternative commercial sources of NR and NRL, as they can be cultivated in the United States and have comparable or superior physical properties to *Hevea* NRL (Junkong, Cornish, & Ikeda, 2017).

2.1.2. Hevea brasiliensis

The rubber tree (*Hevea brasiliensis*) is currently the world's primary source of commercial NR. *Hevea* trees are native to the Amazon region of South America, but also thrive in the tropical climates of Eastern Asian countries such as Thailand, Indonesia, and Vietnam and in equatorial African countries like Cameroon and Cote D'Ivoire. From 2000 to 2022, total global rubber consumption rose from 17.9 million metric tons to 29.6 million metric tons, and the demand for rubber is expected to continue rising (Malaysian Rubber Board, 2023). Because NR is essentially produced from a single source, supply chains for NR are extremely long and are easily disrupted by weather, politics, and diseases.

The ever-increasing demand for NR raises serious concerns about the sustainability of *Hevea* as the major global commercial rubber crop. Not only is *Hevea* produced as clones, but the trees are grown as contiguous monocultures, making them highly susceptible to disease spread (Cornish, 2017). *Hevea* trees are also tapped by hand, making the poorly paid harvesting process laborious and time-consuming. As a result, many growers in Asia are replacing their rubber trees with less labor-intensive crops such as oil palm (Cornish, 2017). The increasing demand coupled with the decreasing supply of *Hevea* rubber indicates that a rubber shortage could be on the horizon if current trends continue.

The latex produced from rubber trees contains proteins that can induce Type I latex allergies, and accelerants added to the rubber during the manufacturing process can also induce Type IV contact dermatitis (de Groot et al., 1998). Healthcare workers are at

especially high risk of developing a latex allergy, as latex gloves are worn in up to 98% of healthcare procedures performed in the United States (Zak et al., 2000).

2.1.3. Parthenium argentatum

Guayule (*Parthenium argentatum*) is shrub native to the Chihuahuan Desert of the northern region of Mexico and the southwestern United States. Unlike the rubber tree, guayule can be cultivated domestically, which would reduce the United States' dependence on foreign countries and geographically diversify the natural rubber supply. Guayule shrubs store rubber particles in the parenchymatous tissue of their bark in individual cells, which means that they cannot be tapped like rubber trees. Instead, the plant cells must be ruptured through mechanical processes such as blenders, roll mills and extruders (van Beilen & Poirier, 2007).

Guayule latex (GNRL) is unique because its proteins are not cross-reactive with those of *Hevea* latex, indicating that it is a safe NR alternative for people with existing Type I latex allergies (Siler et al., 1996). Medical products made from GNRL, such as gloves and condoms, have also demonstrated highly effective barrier properties, making them safer than medical products made from conventional materials (Cornish & Lytle, 1999).

Other unique properties of GNRL films include higher tensile strength and lower modulus than both synthetic rubbers and other natural rubbers (Nguyen et al., 2007). These properties make GNRL the ideal material for medical devices such as gloves because it produces simultaneously the strongest and the softest variety of latex film.

2.1.4. Taraxacum kok-saghyz

Taraxacum kok-saghyz (TK), or the rubber dandelion, is native to Kazakhstan, Kyrgyzstan, and Uzbekistan. These plants grow best in temperate climates, and so can be cultivated in the northern region of the United States. As with guayule, the domestic cultivation of TK has the potential reduce the U.S.'s reliance on Southeast Asian countries for natural rubber.

Unlike *Hevea* or guayule plants, TK plants produce latex (TNRL) in the laticifers of their root systems. The rubber and latex can be harvested by a number of different methods (Salehi et al., 2022), including those adapted from guayule (King-Smith et al., 2023).

TK latex (TNRL) contains multiple proteins that cross react with antibodies raised against *Hevea* latex proteins (Cornish et al., 2015). As in *Hevea* latex products, the leaching process alone is not sufficient to remove the bound proteins found in TK latex, and thus it may still induce a reaction in people with existing *Hevea* latex allergies.

The properties of TK make it an ideal material for manufacturing tires because it has been demonstrated to be as resilient as *Hevea* tires while also reducing the environmental impact of the tire industry. Several manufacturers, including Continental Tire, are currently developing commercial tires made from rubber dandelion latex as a more sustainable alternative to traditional tires (Continental Tire).

A summary of the similarities and differences between the rubber tree, rubber dandelion, and guayule is shown in Figure 2.1.

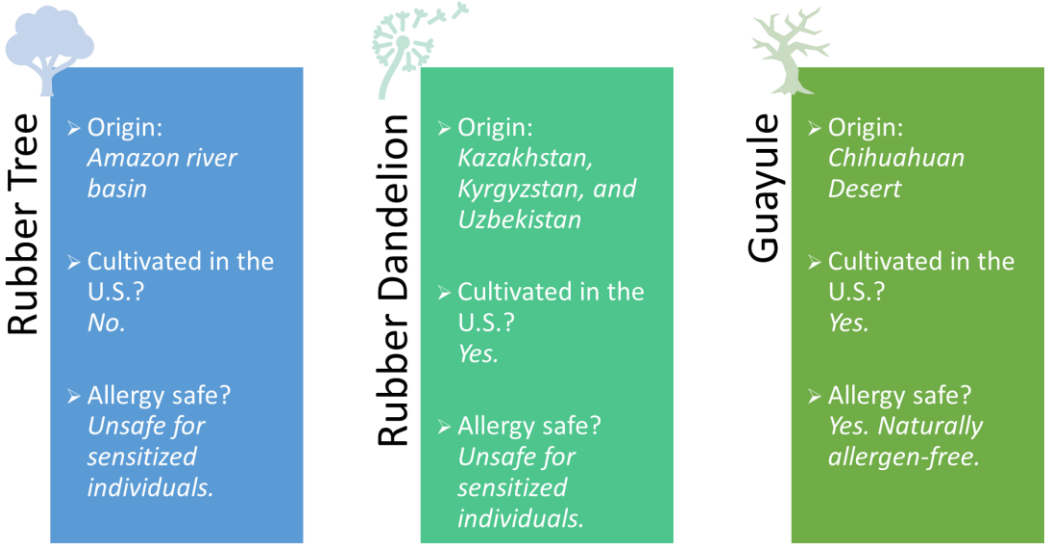


Figure 2.1. Comparison of the rubber tree, rubber dandelion, and guayule.

2.1.5. Synthetic Rubber

The development of synthetic rubber was accelerated during World War II when Japan overran the rubber plantations in Southeast Asia, cutting off the allies' rubber supply (Morton, 1981). Today, synthetic rubber remains a popular material because it is free of protein allergens.

Synthetic rubber comes in many versions, but all are made primarily from petrochemicals. Styrene-butadiene rubber (SBR), which is synthesized from the co-polymerization of styrene and 1,3-butadiene, is one of the most common varieties of synthetic rubber. SBR has been used in a wide variety of products, including tires, shoes, gaskets, and even chewing gum (Obrecht et al.).

Other common varieties of synthetic rubber include polyisoprene, which is synthesized through the polymerization of isoprene, neoprene, which is synthesized

through the polymerization of 2-chlorobutadiene, and nitrile, which is synthesized through the polymerization of 2-propenenitrile and butadiene.

Synthetic rubber products are often more resistance to oils and solvents than NR, but cannot match the mechanical properties of NR (Abraham & Ramesh, 2002). When used in medical devices, synthetic latex poses its own threat to public health due to its inferior barrier efficiency, low tear resistance, and sometimes low strength.

2.2 Sustainability

Several factors contribute to the sustainability of rubber products, including water and land use, shipping/transportation, processing, and disposal. Rubber waste takes a particularly long time to degrade due to its sulfur crosslinked chemical structure and the presence of stabilizers and other additives (Shah et al., 2013). However, both natural and synthetic rubber can be broken down by specialized species of microorganisms (Shah et al., 2013).

A life cycle analysis study comparing guayule, *Hevea*, and synthetic rubbers found that guayule had a lower ozone depletion impact than synthetic rubber and lower global warming and acidification potentials than *Hevea* rubber (Soratana et al., 2017). However, the only instance of a published net positive energy scenario was *Hevea* rubber and biodiesel co-production, which produced a net gain of 3.25 MJ/kg rubber (Soratana et al., 2017).

Rubber tree plantations and rubber processing facilities have caused a huge strain on natural resources such as water and land in Southeast Asia, as discussed in detail in

Chapter 3. The unsustainable nature of rubber production in Southeast Asia necessitates the transition to more environmentally sustainable sources of NR, such as guayule or rubber dandelion. These alternatives are already needed to meet projected increases in NR demand.

2.3. Safety

2.3.1. Latex Allergies

An essential distinction between natural and synthetic rubber is the ability (or lack thereof) to induce systemic (Type I) latex allergy. A Type I allergy is a hypersensitivity reaction in which the body releases the antibody immunoglobulin E (IgE) in response to a particular antigen, which causes a chain reaction ending with the release of histamines and ultimately anaphylactic shock (Cornish, 2012). In the case of natural rubber, a person is sensitized via exposure to large amounts of immunogenic proteins. Once sensitized, any additional exposures, even of trace protein amounts, can cause a potentially fatal allergic reaction. The fear surrounding latex allergies is the main cause of the shift from NR products to synthetic products in healthcare facilities (Cornish, 2012).

Immunogenicity is defined as the induction of a cell-mediated immune response, while antigenicity is the combination of the final products of the immune response, such as antibodies and surface receptors on T cells (Zhang & Tao, 2015). Latex-induced allergic reactions are classified as both immunogenic and antigenic due to the immune system's creation of antibodies in response to antigenic latex proteins. This means that upon initial exposure, the immune system becomes sensitized to latex proteins and begins

building an immune response through the generation of IgE (Actor, 2023). Upon subsequent exposures to any relevant antigen, a full immune response is triggered, possibly without the person's knowledge of their sensitivity. The resulting allergic reaction can range from mild skin irritation to life-threatening anaphylaxis. The Lowry method is a technique used for quantifying the protein content of a sample; however, antibody tests and antigenic protein tests (ASTM D6499) are required to quantify the antigenic protein content of natural latex (ASTM International 2018).

Fortunately, if the leaching process is performed correctly, most natural rubber products will not contain enough soluble proteins to sensitize a person to latex proteins, (Cornish, 2012) although they can still trigger dangerous reactions in previously sensitized patients. Therefore, in many cases, latex sensitization can be traced back to a lack of oversight or integrity in the medical glove manufacturing process.

Unleached powdered gloves posed a particular threat prior to the powder ban by the U.S. Food and Drug Administration (FDA) in 2017. Latex proteins on unleached gloves migrate out and bind to the powder on the gloves (Field, 1997). Frequent donning and removal of these gloves caused the powder-bound proteins to become aerosolized, allowing them to be inhaled by healthcare workers and patients (Field, 1997). Although the FDA requires gloves to be properly leached, low inspection rates make enforcement challenging.

An additional example of the dangers of unleached natural latex products is their use in dentistry. In one study, a random sampling of commercially available *Hevea* latex dental dams contained multiple products with protein levels high enough to likely induce

a Type I latex allergy in a non-sensitized person, or a severe allergic reaction in a person who had been previously sensitized (Cornish et al., 2019). Sensitization risks are especially high with unleached dental products because the allergenic *Hevea* proteins are soluble in saliva, which is absorbed by the patient through mucosal membranes.

The latex protein levels in guayule latex are too low to induce an immunogenic response, which means that guayule is safe for those with existing latex allergies (Cornish, 2012; Hamilton & Cornish, 2010). On the other hand, TNRL contains these cross-reactive proteins and should be avoided by individuals with Type I latex allergies (Cornish et al., 2015).

Hevea latex and synthetic latex products have also been demonstrated to induce Type IV contact dermatitis, which is a delayed hypersensitivity reaction in the skin (Zak et al., 2000). Type IV reactions are caused by the preservatives, vulcanizing agents, and accelerators used during the manufacturing process (Zak et al., 2000). There are two types of contact reactions: allergic contact dermatitis, where the body responds to an antigen with an allergic reaction, and irritant contact dermatitis, where the body responds to an irritating substance by inducing a rash. Hypoallergenic accelerators have been developed to mitigate contact dermatitis reactions in those who frequently come into contact with natural latex products (Ramirez Cadavid et al., 2022).

2.3.2. Product Performance

The physical properties of film products made from natural latex are generally far superior to those made from synthetic latex, although synthetic polyisoprene has been used as an analog. For instance, medical gloves made from natural latex exhibit high

tensile strength and elongation to break, low modulus, making them softer and more comfortable, high barrier efficiency, meaning that they do not inherently have holes or punctures, and the ability to form crystallites under strain, making them tear resistant (Abraham & Ramesh, 2002). Gloves made from GNRL have superior barrier efficiency against viruses, including the φX174 virus: a model virus with a diameter of 27 nm, which is smaller than the smallest known human pathogenic virus (Cornish & Lytle, 1999). Even a pinhole-sized perforation is large enough for pathogenic viruses and bacteria to pass through the protective barrier of a medical glove, rendering it ineffective. Therefore, high durability and mechanical performance are crucial for barrier-providing products such as gloves and condoms.

The superior performance of NRL is due in part to the presence of non-rubber aggregated components, such as proteins, that act as natural reinforcing fillers, expediting polymer chain orientation and strain-induced crystallization (Junkong, Cornish, & Ikeda, 2017). Strain-induced crystallization, which only occurs in natural latices, is a strengthening effect caused by the alignment and subsequent crystallization of polymer chains (Ikeda et al., 2016). The rigid crystallites prevent the propagation of tears in the latex product, making it more resilient.

A study in which surgical gloves were collected and analyzed for perforations following orthopedic surgeries found none of the synthetic gloves were suitable for surgery due to either poor handling properties or high perforation rates (Thomas et al., 2011). Another study analyzing the barrier efficiency of natural and synthetic latex

gloves found that the increased elasticity of natural latex gloves allowed them to self-close upon perforation and maintain their barrier integrity (Bardorf et al., 2016).

2.5. Rubber in the Medical Field

Natural rubber products, such as gloves, catheters, breather bags, surgical tubing and balloons, and dental dams, were used safely in the medical field for decades prior to the 1980s. During this time period, the demand for personal protective equipment increased suddenly, from 2 billion/year to 30 billion/year in response to the AIDS epidemic (Cornish & Brichta, 2002). To meet this demand, many inexperienced glove manufacturers entered the market and either diminished or completely eliminated the leaching step - the process by which soluble latex proteins are removed latex products at the gel stage (Cornish & Brichta, 2002). As a result, many Americans developed life-threatening Type I latex allergies. In 1989, for instance, the FDA reported that 16 people died of latex allergies caused by the latex cuffs used on the tip of barium enema catheters (Roy, 2000). Today, around 30 million Americans have IgE antibodies against *Hevea* latex proteins and so are at risk of dangerous reactions to NR and NRL products (Cornish et al., 2019).

The surge of Type I latex allergies in the U.S. caused the healthcare industry to transition to synthetic materials. While these materials are safer for latex-sensitive individuals, the mechanical properties of synthetic latex products, such as modulus, tensile strength, and barrier efficiency, are substandard compared to NR products (Abraham & Ramesh, 2002). To ensure that these underperforming synthetic latex

medical products could be sold in the United States, agencies such as ASTM International and the FDA reduced the minimum physical requirements for medical products made from synthetic latex.

The demand for medical gloves doubled in 2020 due to the COVID-19 pandemic, and, just as in the 1980s, many inexperienced glove manufacturers from overseas entered the market to capitalize on this high demand (*Medical Device Shortages List*). Unfortunately, as demonstrated in Chapter 6, many of these gloves were substandard and did not meet the minimum performance requirements of regulatory agencies, jeopardizing the health and safety of healthcare workers. It is not known if any NRL glove manufacturers curtailed the leaching step in their rush to market.

2.6. ASTM International Standards

ASTM International is an organization that sets manufacturing standards for a wide variety of materials, products, and systems. The spike in latex allergies that occurred in the 1980s coupled with the Centers for Disease Control (CDC)'s strict glove mandates to control the AIDS epidemic caused ASTM International to draft new, reduced standards for the substandard synthetic latex gloves that were growing in popularity. For instance, nitrile examination gloves no longer had to adhere to the original requirements set forth for examination gloves in ASTM standard D3578-19, but now had their own standard (D6319-19) with reduced requirements for thickness and ultimate elongation (ASTM International 2019b, 2019e). Reducing the physical requirements for synthetic medical gloves allowed them to enter the U.S. market with fewer restrictions, and so

helped to alleviate the issue of natural latex allergies. However, this benefit also came at a huge cost: medical gloves were no longer providing the same level of protection as they were prior to the 1980s (Abraham & Ramesh, 2002). Thus, a need exists for a medical glove that is as strong and durable as *Hevea* latex but that is also safe for those with latex allergies, and these requirements are fulfilled by guayule latex.

Another ATSM standard that is frequently used to analyze the safety of natural latex products is the modified Lowry assay standard D5712-15 (ASTM International 2020b). This technique is used to quantify water extractable protein levels in NRL products and can be used to quantify the total protein in latex emulsions. This is a valuable tool for determining whether a particular variety of NR product contains potentially sensitizing levels of latex proteins. The Lowry method has been used in previous studies to analyze the protein content of *Hevea*, guayule, and TK latecies (Cornish et al., 2006; Cornish et al., 2015).

2.7. Specialty Biomedical Rubber Products

Rubber is used in a wide range of medical products that are utilized both internally and externally to the human body. Examples of internal devices include intravenous catheters, drainage tubes, and artificial heart valves, and external devices include medical gloves, tapes, and orthopedic casts (Yoda, 1998). Elastomers used in biomedical applications must be sterilizable, biocompatible, and durable for the safety of the user, which makes natural latex an ideal material for biomedical devices (Andrade et al., 2022; Yoda, 1998).

Many external biomedical elastomeric products, such as gloves, provide life-saving protective barriers for healthcare providers and patients alike. Medical gloves and other personal protective equipment (PPE) prevent the spread of healthcare-associated infections (HAIs), which are diseases that a patient does not have at time of admittance to a healthcare facility, but rather acquires during their stay at the facility. The importance of medical gloves in the prevention of HAIs was highlighted during the COVID-19 pandemic when PPE shortages were prevalent.

Another specialized rubber medical device is the endotracheal tube (ETT) balloon cuff. This device, which is commonly made out of PVC, is a balloon that attaches around the endotracheal tube. The balloon is inflated to hold the ETT in place in a patient's trachea and ideally creates a seal between the ETT and a patient's tracheal wall (Hamilton & Grap, 2012) to prevent drainage of bacteria-laden saliva into the lungs. Until Type IV latex allergy, a complete seal was usually achieved. However, PVC is a plastic, not an elastomer, and the PVC balloon can only make a perfect seal if it is fully inflated size exactly matches the size of a patient's trachea. In practice this does not occur because larger balloons are used to ensure that the ETT is held in place. Thus, the inflated balloons have remaining pleats through which saliva can pass into the lungs and may cause a pulmonary disease known as ventilator associated pneumonia (VAP). Perforated balloons also can cause VAP. Research has shown that 8% to 28% of mechanically ventilated patients develop VAP (Hamilton & Grap, 2012). The financial burden of treating VAP is estimated to be between $10,000 and $40,000 per patient in the United States (Luckraz et al., 2018). ETT cuffs can also cause severe tracheal damage if they are

overinflated (Moon et al., 2022). Therefore, inflating the cuff to the recommended range of 20–30 cm H_2O is essential for patient safety (Moon et al., 2022). An ETT cuff made from soft, durable natural rubber such as guayule latex can alleviate the issues associated with ETT cuff inflation and performance without causing Type I or Type IV allergies or irritant reactions in the tracheal wall.

Chapter 3. Environmental Impacts of *Hevea brasiliensis* Rubber Production in Southeast Asia

This chapter provides an overview of the negative environmental impacts of the Brazilian rubber tree (*Hevea brasiliensis*) on land, water, soil, and biodiversity in Southeast Asia where the crop is mainly cultivated. The objective of this chapter is to elucidate the current ecological footprint of the rubber industry in order to emphasize the need for an alternative, sustainable source of natural rubber such as the guayule shrub (*Parthenium argentatum*) or rubber dandelion (*Taraxacum kok-saghyz*).

3.1. Introduction

Hevea brasiliensis, commonly known as the Para rubber tree, is the primary source of the natural rubber used to manufacture everything from car tires to condoms. Although native to South America, the rubber tree grows well in most tropical environments, including the forests of Southeast Asia. In fact, around 89% of the world's rubber is grown and produced in Southeast Asia, with production expanding by nearly 1500% from 1961 to 2011 (Ahrends et al., 2015; Li & Fox, 2012). While this rapid expansion has had positive effects such as providing steady work for low-income farmers and factory workers, the resulting impact on the environment has been devastating. The objectives of this review chapter are to discuss the negative impacts of rubber plantations

and manufacturing facilities in Southeast Asia, and to identify ways in which these impacts can be mitigated.

3.2. Impact of Rubber Plantations

3.2.1. Land conversion

When rubber trees are grown in non-tropical environments, their potential for rubber production greatly decreases (Zomer et al., 2014). One study comparing the geographical distribution of historically suitable environments for rubber tree growth to the actual location of rubber plantations in 2010 found that 72% of plantations were grown in suboptimal environments (Ahrends et al., 2015). These environments were considered suboptimal due to their high altitude, cold temperatures, steep slopes, and short wet seasons. Another study identified a correlation between rubber growing areas and land use classification; the largest amounts of rubber being grown in the zones classified as Extremely Hot/Mesic and Extremely Hot/Moist; however, encroachment was evident into less suitable upslope areas (Zomer et al., 2014).

Rubber trees in China, for example, are grown as far north as 22 degrees latitude (Li & Fox, 2012). Yunnan was identified as the province with the most dramatic change in land use, with 71% of the total area of rubber trees under 4 years old being found in the province. A possible explanation for the spread of rubber plantations to higher altitudes is climate change. In Xishuangbanna, Yunnan, China, for instance, where rubber production is currently limited by bioclimatic barriers, approximately 75% of the total area of the prefecture is predicted to have the climate conditions suitable for rubber production by

2050 (Zomer et al., 2014). Global warming acts as a catalyst for the expansion of rubber plantations because it causes previously unsuitable, high-altitude lands to become more suitable for rubber tree growth.

Another catalyst for the spread of rubber plantations, without clear-cutting virgin rain forest, is the market price for rubber. A trend exists between the number of rubber plantations in Southeast Asia and the value of rubber, with rubber prices tripling between the years 2001 and 2011 (Ahrends et al., 2015). The high global demand for rubber is yet another incentive for Southeast Asian farmers to cultivate this crop.

3.2.2. Biodiversity

Land conversion and expansion of rubber plantations beyond traditionally suitable environments has drastically reduced the biodiversity in many species-rich areas of Southeast Asia. Many new rubber tree plantations are monocultures, or single-species plantations (Ahrends et al., 2015). Monocultures reduce biodiversity by restricting the local food chain and by replacing highly biodiverse environments, such as tropical forests.

Monocultures limit the biodiversity of an area indirectly through the food chain. By restricting the variety of available nutrients for primary consumers, the available nutrients for secondary consumers is also restricted. An example of this effect was found by studying the diversity of insectivorous bats in southern Thailand. The researchers were able to identify 19 different bat species in forests, but only 10 varieties were found in rubber plantations; a result which correlated with the insect biomass of the respective

study area (Phommexay et al., 2011). The lack of biodiversity effectively created a "floristic impoverishment" for both bats and the insects they prey upon (Phommexay et al., 2011).

As the total area of monoculture rubber plantations in East Asia continues to grow, the area of tropical forests and other habitats for native species is greatly reduced. For example, from 1975 to 2014, forest area in China decreased from 69.31% to 57.81%, while plantations expanded from 0.52% to 12.71% (Liu et al., 2017). This trend is also very marked in Thailand and Malaysia. This loss of biodiversity resulted in Asian elephants occupying only 5% of their original habitat (Liu et al., 2017). As a result, many areas in southern China experienced an increase in poaching and elephant-farmer conflict as these animals encroached onto farmlands to forage for food beyond their highly fragmented habitat (Liu et al., 2017). Similarly, the number of livestock such as buffaloes raised by farmers in Menglun, China dropped from 5260 in 1988 to fewer than 700 in 2003 due to their tendency, much like Asian elephants, to destroy rubber seedlings (Liu et al., 2006).

3.2.3. Water and soil

The impacts of rubber plantation expansion go beyond conservation, and a primary example is the rubber tree's lack of efficient water use. *H. brasiliensis* is a drought-avoidant plant that readily uptakes and stores water to cope with seasonal drought (Wu et al., 2016). While this strategy allows the plant to survive in harsh conditions, it has also resulted in reduced water supplies in many small Asian villages

that cultivate rubber (Wu et al., 2016). The fact that many of these plantations are monocultures further exacerbates this issue, as the trees have no competition for water and may therefore thrive despite their water-use inefficiency.

Another impact of rubber tree expansion is poor soil quality. Long-term rubber farming results in soil acidification, nutrient depletion, and soil compaction (Zhang & Zhang, 2005). Soil compaction is particularly alarming because it causes the soil to become more sensitive to water erosion (Zhang & Zhang, 2005).

3.3. Impact of Rubber Production Facilities

3.3.1. Water Contamination

Facilities that manufacture rubber products in Southeast Asia also contribute negatively to the environment. One of the most serious environmental concerns is the discharge of untreated effluent from these factories into nearby water sources. Untreated wastewater is toxic, and it effectively poisons the water supplies in which it is released. A survey of several small cooperative rubber sheet factories in southern Thailand found that despite the country's regulations against the discharging of untreated effluent, many factories failed to meet basic standards due to lack of finances and workers with maintenance knowledge (Chaiprapat & Sdoodee, 2007).

3.3.2. Ecological Footprint

An ecological footprint (EF) is, "an indicator used to represent the total land and water ecosystem requirements for providing resources and absorbing emissions in the

unit of global hectare (gha) per functional unit of products" (Musikavong & Gheewala, 2017). In other words, an ecological footprint accounts for the use of resources such as water, land, and energy, as well as emissions such as carbon dioxide and other pollutants.

Because the manufacturing process for different types of rubber products use somewhat disparate resources, their respective ecological footprints also differ. For example, the EF for the production of ribbed smoked sheets, which are used in car tires and industrial rubber parts, is 6.78 gha/ton, while the EFs to produce the block rubber found in belts and shoes and the concentrated latex found in medical gloves and condoms are 7.06 and 5.07 gha/ton, respectively (Musikavong & Gheewala, 2017). This means that the process of rubber production for these products demands 6.78, 7.06, and 5.07 times the resources that the ecosystem is able to replace. Therefore, the current method of rubber production is highly unsustainable.

3.4. Mitigating Impacts

Many of the environmental issues created by rubber plantations and production facilities can be mitigated through a small number of universal solutions. The most essential solution for the prevention of additional land conversion and water pollution is government regulation and enforcement. Unless regulations are put in place, the economic benefits of growing rubber are likely to continue to drive rubber tree expansion in Southeast Asia (Liu et al., 2006). In the case of rubber production facilities, existing laws must be properly enforced to minimize damage to the environment. The most effective way to reduce the ecological footprint of these factories is to implement policies

that will optimize the production process and closely manage both wastewater and water usage (Musikavong & Gheewala, 2017).

Effluent recycling is another important tool that can reduce the pollution of water sources near rubber production facilities in Southeast Asia. When effluent from small cooperative rubber sheet factories is used to water rubber trees, their latex yield is nearly double that of rain-fed rubber trees (Chaiprapat & Sdoodee, 2007). Effluent can also be safely used to grow edible crops such as rice and cucumbers, once treated (Chaiprapat & Sdoodee, 2007).

Agroforestry is a technique that can increase the biodiversity of rubber monocultures by combining agriculture and forestry techniques (Wu et al., 2016). By intercropping beverage plants such as coffee, tea, and cocoa trees among rubber trees, not only do the plants use water more efficiently due to interspecies competition, but they also produce larger rubber and biomass yields (Wu et al., 2016). Another advantage of agroforestry is that it can support a wider range of consumers. Agroforests can harbor bat species that prefer to fly in cluttered spaces in addition to those that prefer open spaces (Phommexay et al., 2011). These more diverse plantations also allow for a greater diversity of insects, the primary food source for bats. In addition, intercropped plantations are also known to have reduced soil and nutrient erosion compared to monoculture plantations.

To protect species that are threatened by poaching, such as the Asian elephant, conservation corridors should be created in addition to forest restoration efforts. Corridors, “expand the range of suitable habitats by connecting isolated patches of land,

reducing human-elephant conflicts, and increasing population size, including gene flow exchange" (Liu et al., 2017). This means that the number of Asian elephants that encroach onto farmland will be reduced, as their habitat will become less fragmented by rubber plantations.

The final method to reduce the environmental impacts of rubber production and processing is education. It is essential that farmers and factory workers are aware of the environmental impacts of rubber production, and the most effective ways to mitigate their ecological footprints. Awareness of these environmental issues in the general population may also create increased social pressure for governments to regulate rubber production more closely. Therefore, education is one of the most essential tools for reversing current trends in rubber production.

3.5. Conclusions

Several environmental issues result from rubber production in Southeast Asia. The expansion of rubber plantations into suboptimal environments causes a decrease in rubber yield, biodiversity, and soil quality, and an increase in habitat loss and soil degradation. The lack of regulation of rubber processing facilities results in the pollution of local water sources and the draining of natural resources in a way that is not ecologically sustainable. The potential solutions to these issues include increased government regulation, effluent recycling, the implementation of agroforestry, the creation of conservation corridors, and education of those who work in the rubber industry and the general public. In addition, investing in alternative sources of natural

rubber such as guayule (*Parthenium argentatum*) and the rubber dandelion (*Taraxacum kok-saghyz*), both of which can be cultivated in the United States, would diversify the natural rubber supply and reduce the rubber industry's strain on the environment.

Chapter 4. Invention of a Medical Glove Durability Testing Device

This chapter is based on the following publication:

Venturini, A., Pancake, M., VanCleave, W., Wan, Y., & Cornish, K. (2022). Invention of a medical glove durability assessment device. Inventions, 7(3), 62. https://doi.org/10.3390/inventions7030062 (Peer Reviewed)

The purpose of this chapter is to provide the specifications for an automated glove durability testing device, with the goal of implementing it a part of an ASTM International standard on glove durability. The device provides glove manufacturers with an objective means of evaluating glove durability to ensure consumer safety. As the first author of this article, I guided specifications for glove tester, designed the experiment, collected and analyzed the data, and drafted the manuscript.

4.1. Abstract

Healthcare workers across the globe rely on medical gloves to prevent the transfer of harmful bacteria and viruses between themselves and their patients. Unfortunately, due to the lack of an in-use durability standard for medical gloves by the American Society for Testing and Materials, many of these gloves are of low quality and are easily torn or punctured, exposing wearers and patients to potentially deadly diseases. To solve this problem, a device that automatically detects material failures the size of a pinhole during active testing was invented. The device consists of a prosthetic hand, vacuum pump,

mobile textured roller, pressure sensor, and liquid spray system. It works by creating a vacuum inside the glove and repeatedly moving the textured roller into contact with the fingertips, which, on the prosthetic hand, are porous. When a glove perforates, the vacuum is broken, pressure within the hand rapidly increases, and the operator is alerted on a touchscreen that the glove has failed. In addition, the liquid spray system allows the user to test gloves in "real world" conditions, because healthcare workers often come into contact with liquids that may alter glove durability. As a preliminary test of the device's accuracy, five nitrile and five latex exam gloves were tested using the system's default settings. Natural latex is known to be the highest performing glove material, so the nitrile gloves were expected to fail more quickly than the latex gloves. The test results concur with this expected order of failure: nitrile first, with an average failure time of 300 seconds and 42 average number of roller touches, followed by natural latex, with an average failure time of 2,206 seconds and 300 average number of roller touches. These results provide evidence that the device accurately ranks glove durability, and therefore could be used to develop an ASTM durability standard and improve the quality of gloves made from different polymers.

4.2. Introduction

Medical gloves are an essential piece of personal protective equipment (PPE) because they act as a protective barrier, preventing the transfer of bacteria, viruses, and toxins from healthcare worker to patient and vice versa. With the emergence and spread of COVID-19 in early 2020, the demand for medical gloves doubled, resulting in many

healthcare facilities facing a shortage of these necessary supplies (*Medical Device Shortages List*; *Medical Gloves Market - Global Outlook & Forecast 2022-2027*). Despite the important role of gloves in disease prevention, the American Society for Testing and Materials (ASTM) standards for rubber surgical gloves (D3577-19) and rubber examination gloves (D3578-19) lack a specification for in-use glove durability once the gloves are removed from their packaging by the consumer (ASTM International 2019a, 2019b). Manufacturing and polymer differences mean that some types of gloves are more prone to breakage under stress than others. Unfortunately, the current ASTM standard for the detection of holes in medical gloves only measures the incidence of gloves with holes before their actual use, and this protocol entails merely filling a glove with tap water and observing it for leaks (ASTM International 2019c).

The need for a standardized medical glove assessment device is most evident when natural and synthetic gloves are compared. A 2011 study in which natural latex and latex-free gloves were examined for perforations following surgical use found that latex was perforated only 34.3% of the time, compared to 80% for synthetic polyisoprene (Thomas et al., 2011). An additional study in which gloves of a variety of materials made by different manufacturers were perforated using a standardized procedure found that bacterial passage through medical examination gloves occurred at a 10-fold higher rate in nitrile and neoprene gloves compared to natural latex (Bardorf et al., 2016). In addition, the size of the hole left in the glove after a needle stick puncture was smaller in natural latex films than in nitrile films (Cornish et al., 2001). These results demonstrate that not all gloves provide the same level of protection, and that a uniform durability standard

would ensure that all gloves provide a minimum level of protection regardless of material or manufacturer.

The combination of high glove demand and lack of a durability standard led to our development of a medical glove durability assessment machine. The device closely simulates real-world glove use because a glove is placed on a prosthetic hand, which comes into repeated contact with a roughened surface until a hole is detected in the glove. This device could ensure that all gloves meet a basic standard of durability while being worn and forms the basis for a new ASTM standard for medical and surgical glove durability. We hypothesized that the New Glove Assessment Device would be able to detect pinhole-size punctures in medical gloves without the need for manual glove inspection or water inflation tests.

4.3 Materials and Methods

4.3.1. Capstone Glove Assessment Device (C-GAD)

The glove testing prototype previously described (Michel & Cornish, 2015) was modified in collaboration with the Center for Design and Manufacturing Excellence (CDME) at the Ohio State University due to expired software. Although the basic components of the C-GAD remained the same, an ESP32 Expressif Systems microcontroller with a Nextion Touch Display LED touchscreen was wired to the motor for improved ease of use. The touchscreen displayed the elapsed time, test number, speed, and force of the motor. The hand was also attached to an aluminum rail structure, and the entire system was mounted on a piece of plywood for added stability (Figure

4.1.). The major drawback of this design was the need to visually inspect the gloves for holes, which entailed frequent inspection stoppages and approximately a 5 sec or more delay in break detection (Thomas et al., 2011). Therefore, a new iteration of this glove testing device was designed, with the goal of increasing precision of glove failure data, improving ease of use, and making a machined version which could be readily manufactured.

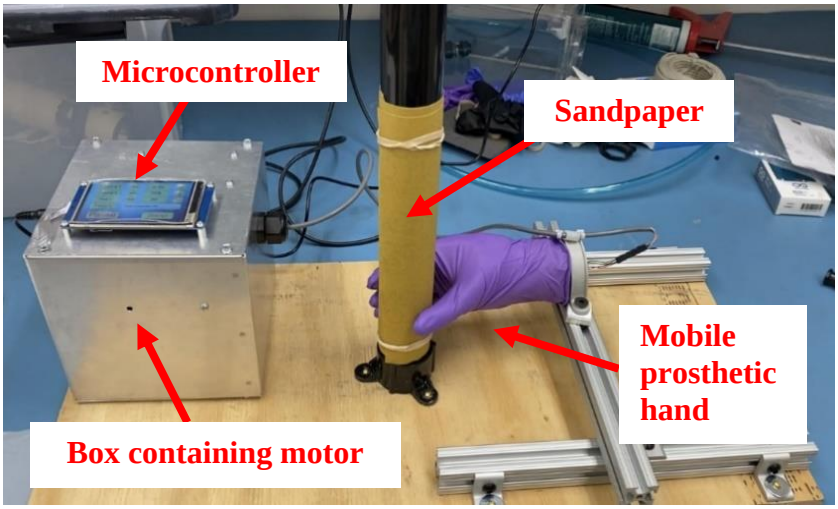


Figure 4.1. Modified setup of the original glove testing device.

4.3.2. New Glove Assessment Device (N-GAD)

4.3.2.1. Touchscreen Display

The N-GAD was designed to automatically detect holes in medical gloves, eliminating the need for manual glove inspection. Like the C-GAD, the N-GAD also utilizes an ESP32 Expressif Systems microcontroller and a Nextion Touch Display LED touchscreen (Appendix A), however, the N-GAD was designed with increased functionality. The homepage of the LED touchscreen (Figure 4.2.) displays the number of

touches completed, the speed of the drum movement in mm/s, the force of the drum in mN, and the number of sprays between touches, and all settings are adjustable (Tables 4.1. & 4.2.).

Figure 4.2. Homepage of LED touchscreen.

Table 4.1. Description of each text field found on the homepage.

ID	Description
t0	Describes what t4 contains and b1 and b5 manipulate
t1	Describes what t5 contains and b2 and b6 manipulate
t2	Describes what t6 contains and b3 and b7 manipulate
t3	Describes what t7 contains and b4 and b8 manipulate
t4	The number of touches the test will execute
t5	The speed the of drum during the test
t6	The force the drum will apply to the glove during the test
t7	The number of touches between each spray, or “OFF” if the spray functionality is disabled

Table 4.2. Description of each button found on the homepage.

ID	Description
b0	Begins a test with the settings as shown on the page
b1	Decrements the number of touches to perform by 1 touch, up to a minimum of 1 touch
b2	Decrements the speed of the drum by 0.1 mm/s, up to a minimum of 0.5 mm/s
b3	Decrements the force of the drum on the glove by 100 mN, up to a minimum of 1000 mN
b4	Decrements the number of touches between each spray by 1 or disables the touch functionality if the current value of t7 is “0”
b5	Increments the number of touches to perform by 1 touch, up to a maximum of 65535 touches
b6	Increments the speed at which the drum will move by 0.1 mm/s, up to a maximum of 10.0 mm/s
b7	Increments the force of the drum on the glove by 100 mN, up to a maximum of 20000 mN
b8	Increments the number of touches between each spray by 1, up to a maximum of 65535, or enables the touch functionality if the current value of t7 is “OFF”
b9	Opens the manual control page

The depressurization failure page appears on the touchscreen if the machine cannot depressurize before a test has begun (Figure 4.3.). This screen has only one text field and one button (Tables 4.3. & 4.4.).

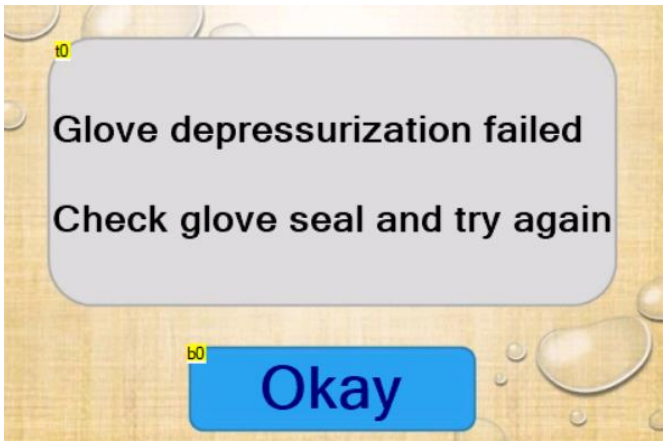


Figure 4.3. Depressurization failure page.

Table 4.3. Description of the text field found on the glove depressurization page.

ID	Description
t0	States that the glove depressurization has failed

Table 4.4. Description of the button found on the glove depressurization page.

ID	Description
b0	Acknowledges the depressurization failure and returns to the home page

The test page appears after the glove has successfully been depressurized and the drum has begun to move. It displays the current elapsed time as well as the touch number that the machine is currently executing (Figure 4.4.). It should be noted that the elapsed time is paused during the process of depressurization. A test can be aborted at any time by pressing the “Abort” button. Otherwise, the machine automatically switches to the “test complete” page once the glove has failed (Tables 4.5. & 4.6.).

Figure 4.4. Test page as it appears during a test.

Table 4.5. Description of each text field found on the test page.

ID	Description
t0	Title field
t1	The current elapsed time of the test, not including depressurization time
t2	The current touch the machine is executing and the total number of touches to execute

Table 4.6. Description of the button found on the test page.

ID	Description
b0	Aborts the test and switches to the abort page

The test abort page is displayed after the “Abort” button has been selected (Figure 4.5.). There are no buttons on this page as its purpose is to inhibit user input until the machine has returned to the pre-test configuration (Table 4.7.). The most time-consuming part of that process is the movement of the drum into the home position. Once the

machine returns to the pre-test configuration, the display automatically switches to the home page.

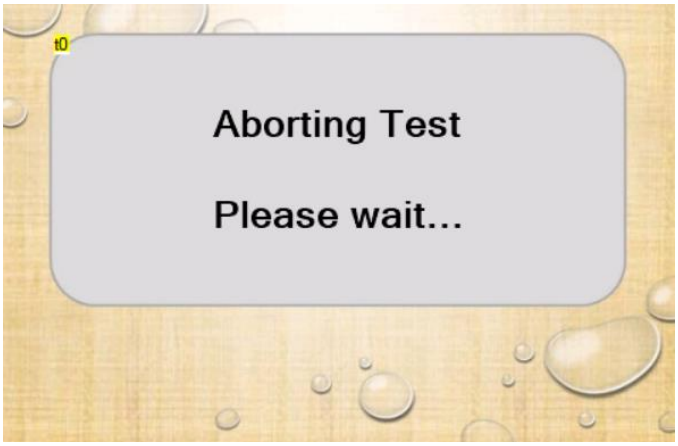


Figure 4.5. Test abort page.

Table 4.7. Description of the button found on the test page.

ID	Description
t0	States that the machine is currently aborting a test

The glove failure page is displayed when a pressure differential is detected by the sensor, indicating that the glove has been punctured. The elapsed time and number of touches are paused so that the user can note them down (Figure 4.6.). Pressing the "Okay" button returns the user to the homepage (Tables 4.8. & 4.9.).

Figure 4.6. Glove failure page with paused elapsed time and touch number.

Table 4.8. Description of each text field found on the glove failure page.

ID	Description
t0	Title field
t1	The elapsed time of the test up until glove failure, not including depressurization time
t2	The current touch the machine was executing when the glove failed, and the total number of touches that were going to be executed

Table 4.9. Description of the button found on the glove failure page.

ID	Description
b0	Returns to the home page

When the number of touches reaches the pre-set value without the glove failing, the “test complete” page is displayed (Figure 4.7.). The elapsed time is paused so that the user can note it down. The machine returns to the home page when the “Okay” button is pressed.

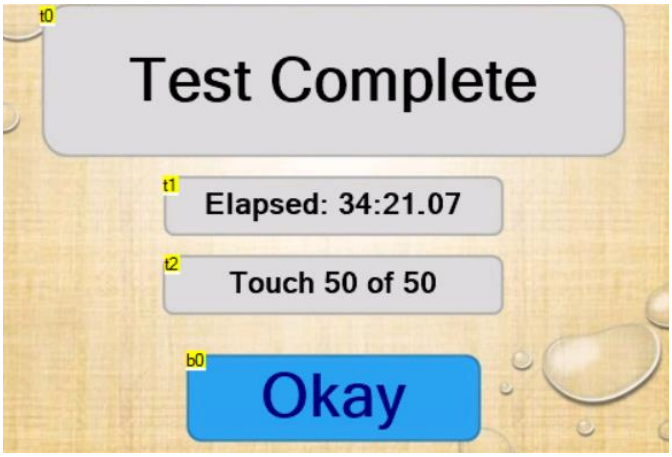


Figure 4.7. “Test complete” page.

Table 4.10. Description of each text field found on the “test complete” page.

ID	Description
t0	Title field
t1	The elapsed time of the test up until the test was completed, not including depressurization time
t2	The current touch number and the total number of touches that were going to be executed, which are the same at the end of a test

Table 4.11. Description of the button found on the “test complete” page.

ID	Description
b0	Returns to the home page

4.3.2.2. System Design

Figure 4.8. shows a conceptual drawing of the basic components of the device. Notably, the new system is encased in plexiglass and contains a pump and reservoir system for testing gloves in wet conditions with various solvents. Another notable

difference from the C-GAD is the stationary prosthetic hand and mobile drum. This design choice was made to allow the prosthetic hand to be easily interchanged with other prosthetic hands of various sizes.

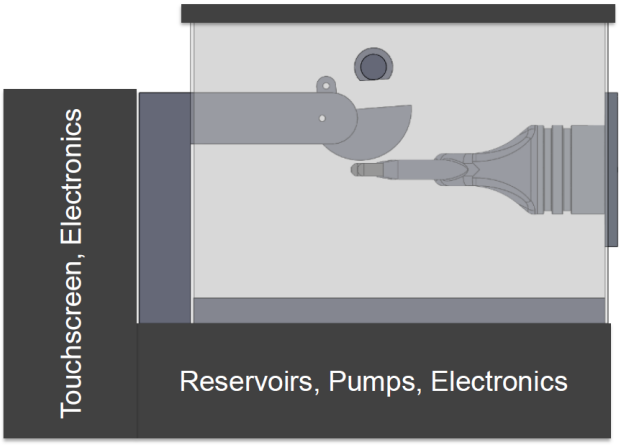


Figure 4.8. Conceptual AutoCAD model of the new glove testing device.

In general, the device works by removing the air from within the base of the prosthetic hand via a vacuum pump after the hand is fitted with a glove. The textured drum then moves into position and comes into contact with the porous fingertips of the hand until a tear occurs in the glove. When this happens, a pressure differential is sensed by a pressure sensor located within the base of the hand, and the device stops, thereby eliminating manual inspection.

4.3.2.3. Hand and Vacuum Pump

For this prototype, a plastic prosthetic hand was 3D printed using the dimensions of an average adult male's hand (Man-Systems Integration Standards). To improve the ease of glove application, the hand was designed without a thumb (Figure 4.9.). The

fingertips of the hand are sintered polyethylene mufflers, which contain intricate networks of open-celled, omni-directional pores that allow for airflow. After being applied to the hand, the glove is held in place with a silicone O-ring, and air is removed from within the base via a 12/24 VDC vacuum pump with a 2-way isolation/exhaust valve (Figure 4.9.). However, when a puncture occurs in the glove, the air is free to flow through the porous fingertips, causing a positive pressure differential that is detected by an Adafruit pressure sensor located within the base of the hand (Figure 4.9.). Prior to installation, the pressure sensor was manually calibrated to ensure accurate results.

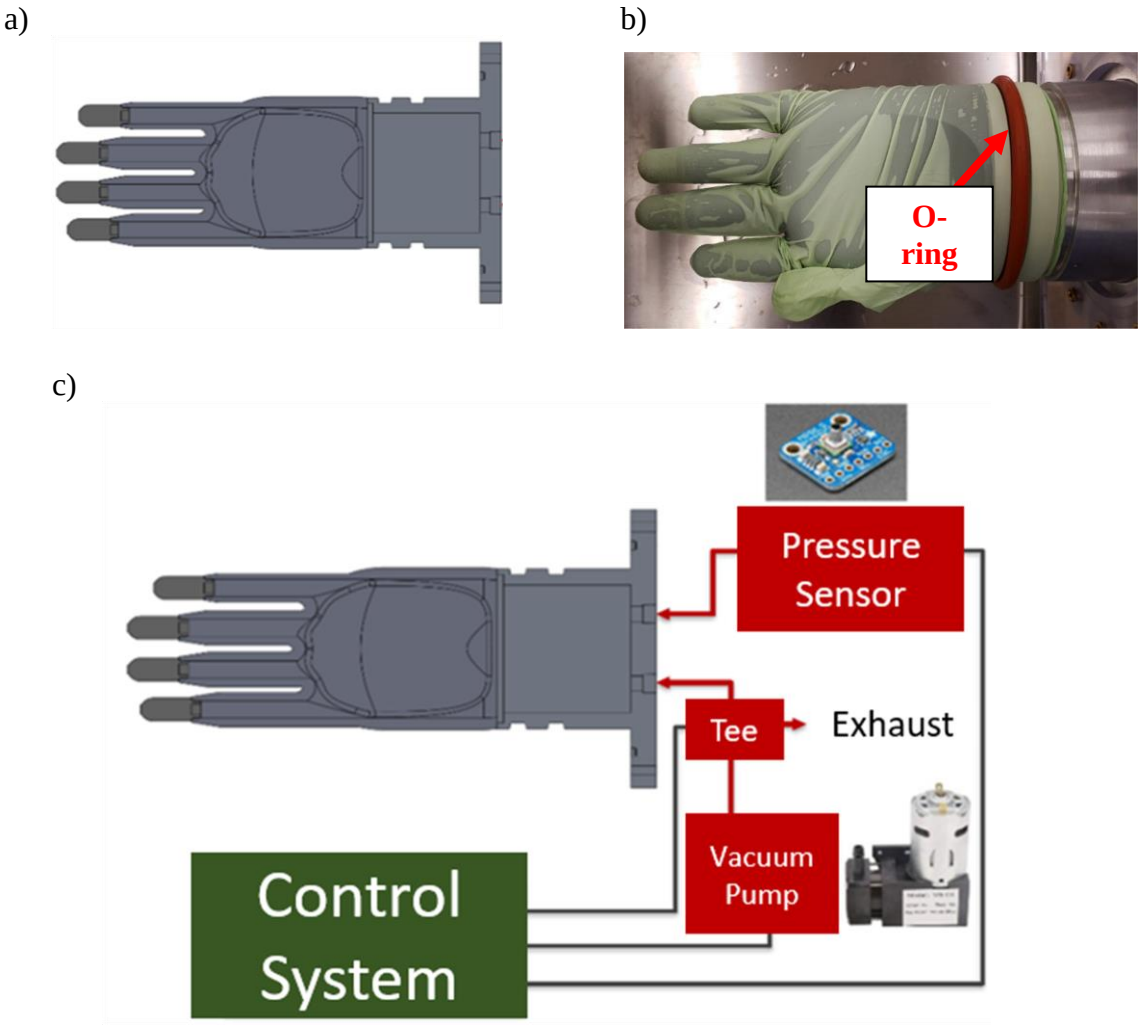


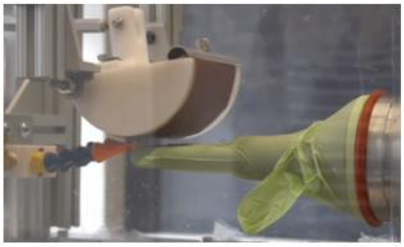
Figure 4.9. a) AutoCAD model of 3D printed prosthetic hand. b) Silicone O-ring applied to the base of the prosthetic hand. c) Diagram of the connections between the prosthetic hand, vacuum pump, pressure sensor, and control system.

4.3.2.4. Drum Motion

The plastic wedge-shaped drum was designed for easy application of sandpaper, which was held in place using two clamps, one on either end of the drum (Figure 4.10.). A stepper motor controlled the movement of the drum by applying a horizontal force to

an attached metal rod. The force caused the drum to pivot around a center pin, creating perpendicular contact with the fingertips of the hand. In order to control the force with which the drum contacts the hand, an in-line 10 kg load cell was calibrated using a second load cell and installed on the same rod that is moved by the stepper motor (Figure 4.10.). Both the stepper motor and the load cell were electronically wired to the control center (Figure 4.11.).

a)



b)

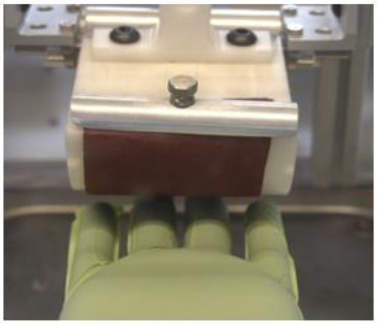


Figure 4.10. a) Side view of drum with sandpaper and clamps, and b) top view of drum with sandpaper and clamps.

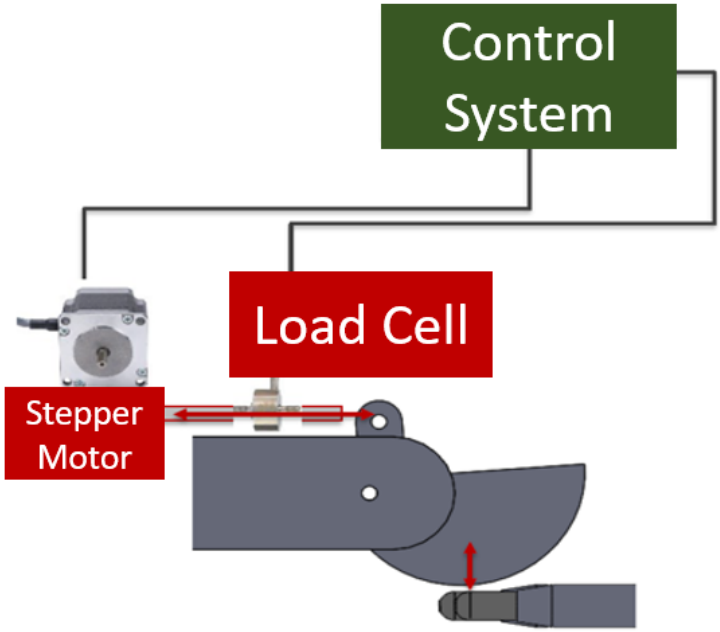


Figure 4.11. Diagram of the connections between the drum, motor, and control system.

4.3.2.5. Liquid System

The liquid system allows to user to test the durability of medical gloves after the gloves are exposed to various solvents. The hand, drum, and spray nozzles were encased in a plexiglass testing chamber to keep the liquid contained during testing (Figure 4.13.). The two spray nozzles were aligned to point at the fingertips of the hand (Figure 4.10.a). The reservoirs were placed within the base of the device, and they consisted of two large plastic bottles with lids containing tubing that connect to either the pump or the liquid-collection pan (Figure 4.12.). A 12/24 VDC peristaltic pump was chosen for the liquid system, and it was connected to the control system so that the user can adjust the number of liquid sprays between touches (Figure 4.12.). The liquid stream was designed to leave the nozzle as a “drip” rather than a spray. This design choice was made to ensure user

safety when performing tests with liquids that are toxic when aerosolized, such as ethanol.

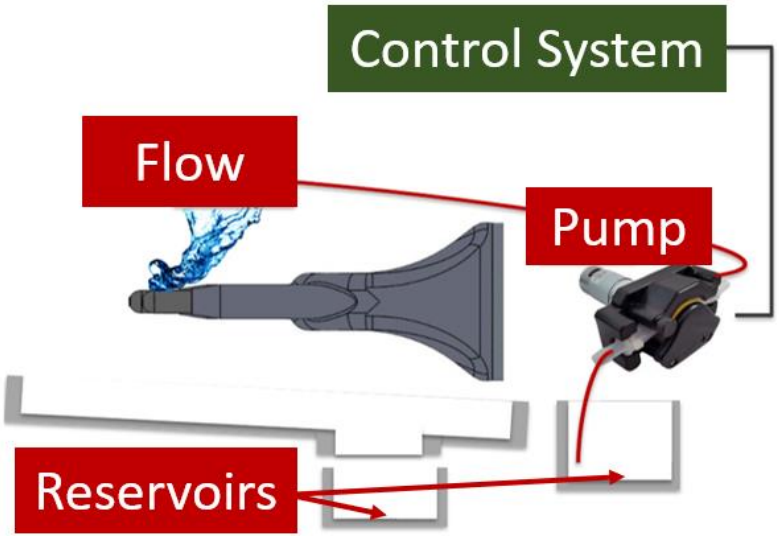


Figure 4.12. Diagram of the connections between the hand, liquid pump, and control system.

In the final assembly of the device, the pumps and reservoir system are located underneath the testing chamber, and the electronic components are located behind the touchscreen to the left of the testing chamber (Figure 4.13.). A complete list of replaceable parts is found in Appendix 5.A. The specifications for the power supply, stepper motor, and pressure are found in Appendix 5.B.

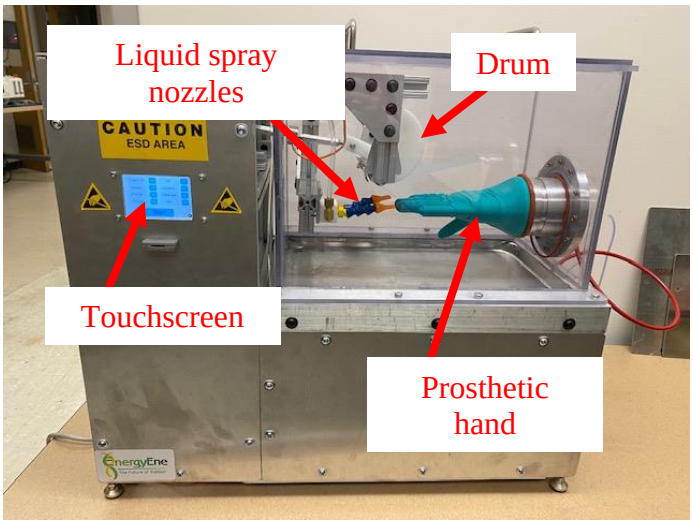


Figure 4.13. Final assembly of the new glove testing device.

4.3.3. Experimental Design

The accuracy of the NGTD was verified by comparing the failure rates of two different exam glove types: nitrile and latex. A previous study found that the failure times of these two glove types were significantly different from each other, with nitrile having the statistically shorter failure time (Michel & Cornish, 2016). Thus, if the NGTD produced failure times that were consistent with these results, the device could be assumed to be accurate. For each trial, the selected glove was carefully placed onto the prosthetic hand through the lid at the top of the testing chamber. The two clamps on either end of the semicircular drum were loosened and a strip of 120-grit sandpaper was clamped in place, one end at a time.

The settings on the touchscreen remained at their default values (Table 4.12.). If a glove did not fail by the end of the 50 touches, the time and number of touches were record and a new test was run. When the glove did fail, the values for elapsed time and

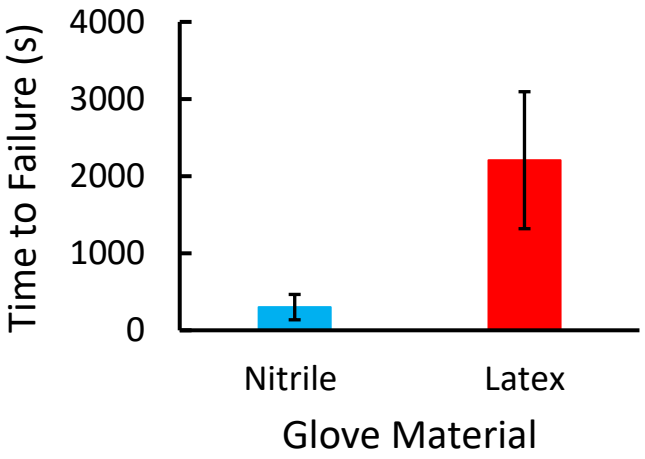
number of touches were totaled and recorded. After failure, the glove was removed from the hand and discarded along with the sandpaper. A new glove and piece of sandpaper was used for each trial.

Table 4.12. Touchscreen settings input for data collection. Note that these are the default settings.

Touch Number	**Speed**	**Force**	**Spray**
50	3.5 mm/s	15000 mN	OFF

4.4. Results and Discussion

a)



b)

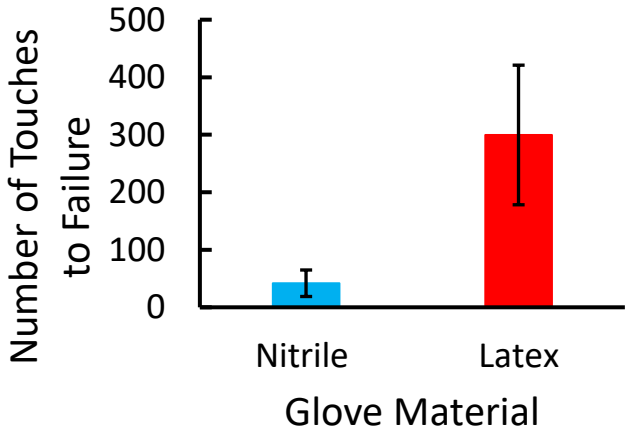


Figure 4.14. a) Failure times in seconds for nitrile and latex examination gloves. The average failure time for nitrile gloves was 300 ± 164 seconds, and the average failure time for latex gloves was 2,206 ± 888 seconds. Each value is the mean of 5 ± SD. b) Number of sandpaper touches to failure for nitrile and latex examination gloves. The average number of touches for nitrile glove failure was 42 ± 23 touches, and the average number of touches for latex gloves was 300 ± 121. Each value is the mean of 5 ± SD.

A one-way analysis of variance test was performed for glove material versus time and glove material versus number of touches (Tables 4.15. & 4.16.). Both of the analyses show that nitrile gloves break more easily than natural latex gloves ($p = 0.0029$ and $p =$

0.0031, respectively). It should be noted that the time and number of touches to failure data for latex has a large variation due to manufacturing inconsistencies, which further supports the need for a universal glove durability standard. The order of glove failure, nitrile followed by latex, concurs with the results of previous studies and provides evidence that the N-GAD's measurements are accurate (Michel & Cornish, 2016).

Table 4.13. One-way analysis of variance of glove material versus break time in seconds.

Source	DF	Sum of Squares	Mean Square	F Ratio	Prob > F
Material	1	9076582	9076582	17.7927	0.0029*
Error	8	4081040	510130		
C. Total	9	13157622			

Table 4.14. One-way analysis of variance of glove material versus number of sandpaper touches to failure.

Source	DF	Sum of Squares	Mean Square	F Ratio	Prob > F
Material	1	166152.10	166152	17.4255	0.0031*
Error	8	76280.00	9535		
C. Total	9	242432.10			

The rise in prevalence of synthetic gloves, especially in the examination glove market, was due to the widespread incidence of Type I latex allergies in the 1990's caused by sensitizing levels of soluble proteins in natural latex gloves. These proteins resulted from a manufacturing failure due to the rapid increase in glove demand in response to the AIDS epidemic. Many new manufacturers sprang up in southeast Asia, and their inexperience led to the elimination of the in-line glove washing process that had previously been the norm. Afterall, latex gloves look exactly the same whether washed or unwashed. After only a few exposures to un-leached high protein gloves, a patient can

develop a permanent Type I latex allergy. However, since this manufacturing failure was characterized and found to be the cause of the Type I latex allergy "epidemic," reputable manufacturers reinstated the inline washing process, and natural latex gloves again became safe for those not previously sensitized by high protein products. Only a few products remain still with high protein levels, such as some brands of dental dams (Cornish et al., 2019). When an unwashed dental dam is placed inside a patient's mouth, the soluble proteins are extracted by saliva in sufficient quantity to sometimes induce sensitization, and certainly enough to cause an allergic reaction in a previously sensitized person (Cornish et al., 2019).

Since medical workers may not be aware of the significant disparity in glove quality, implementing a post-packaging durability assessment as a standard part of the glove manufacturing quality assurance process will ensure that all medical gloves meet a minimum level of durability, protecting the consumer from low-quality gloves. Investing in high-quality gloves may also save healthcare facilities thousands of dollars per year on more expensive life-saving resources. In other words, higher quality PPE protects more people from diseases and hospitalization, can save lives, and reduce medical malpractice claims.

Finally, as the name suggests, natural latex is produced naturally by plants such as *Hevea brasiliensis*, or the Brazilian rubber tree. Plant-based materials are desirable because they are more environmentally sustainable than synthetic materials, which are synthesized from petroleum. Unlike natural latex products, synthetic rubber products are not biodegradable and contribute to the pollution of the environment. The rise in demand

due to COVID-19 also has increased interest in alternative natural latex sources, such as *Parthenium argentatum* (guayule) and *Taraxacum kok-saghyz* (rubber dandelion).

Guayule latex films outperform all other known natural and synthetic latices, including glove durability (Michel & Cornish, 2016), puncture size (Cornish et al., 2001), contain very little protein, and have no proteins which cross react with Type I latex allergy (Cornish, 2012). Rubber dandelion latex appears more similar to rubber tree latex and does contain cross-reactive proteins (Cornish et al., 2015). The introduction of new natural latices makes our device even more relevant to the medical glove industry and their customers.

4.5. Conclusions

The key findings of this study are as follows:

- The average failure time for nitrile gloves was 300 seconds, and the average number of roller touches to failure was 42 touches.
- The average failure time for latex gloves was 2,206 seconds, and the average number of roller touches to failure was 300 touches.
- One-way ANOVA tests showed that nitrile failure time and number of touches to failure were significantly different from latex failure time and number of touches to failure ($p = 0.0029$ and $p = 0.0031$, respectively).

- The order of glove failure, nitrile followed by latex, concurs with the results of previous studies and provides evidence that the N-GAD's measurements are accurate.

Healthcare workers rely on medical gloves for protection against potentially deadly bacteria, viruses, and toxins, but the gloves they use may not actually be providing the level of protection they expect. The medical glove durability assessment device discussed in this paper has the potential to standardize the quality of medical gloves, no matter the material or manufacturer. Regardless of whether the glove is made of synthetic or natural materials, glove manufacturers have a responsibility to produce high-quality gloves with consistent in-use durability. Therefore, future work will include collecting failure data for a wider variety of natural and synthetic gloves produced by different manufacturers and presenting the N-GAD to ASTM as a solution to the lack of durability standard.

4.6. Acknowledgments

This work was made possible through the USDA-NIFA Hatch Project OHO01417 and the engineers and students at the OSU Center for Design and Manufacturing Excellence.

4.7. Addendum

Table 4.15. List of replaceable parts for the N-GAD.

Item	Description	Supplier	Part Number
Liquid Pump	Peristaltic Pump	Simply Pumps	PMP200
Vacuum Pump	Mini Vacuum Pump, 5 L/min, 12V DC	Amazon	753874419842
Valves	Stainless Steel Solenoid Valve, 12V DC, 1/8 NPT	McMaster-Carr	5077T114
Motor	Step Motor Hybrid Linear Actuator, 12V DC	Digi-Key	1568-1189-ND
Load Cell	Mini Tension and Compression Load Cell, 0-10 kg	Amazon	DYMH-103
Pressure Sensor	MPRLS Ported Pressure Sensor, 0-25PSI	Adafruit	3965
Sandpaper	Water Resistant Sanding Sheets	McMaster-Carr	6835A48
O-rings	Soft Silicone O-ring, 1/8, Dash Number 245	McMaster-Carr	1173N484
O-rings	Soft Silicone O-ring, 1/4, Dash Number 411	McMaster-Carr	1173N607
O-rings	Soft Silicone O-ring, 1/4, Dash Number 412	McMaster-Carr	1173N608
O-rings	Soft Silicone O-ring, 1/4, Dash Number 413	McMaster-Carr	1173N609
O-rings	Soft Silicone O-ring, 1/4, Dash Number 414	McMaster-Carr	1173N611
Fingertips	NPT Male Polyethylene Plastic Fitting	McMaster-Carr	4427K82
LED Screen	Nextion Touch Display	Mouser	713-104990604
Stylus	LCD Touch Panels Stylus	Mouser	817-N010-0557-T011

Table 4.16. Power supply characteristics.

	Typical	Maximum Range
Input Voltage*	120 VAC or 230 VAC	85 – 132 VAC or 170 – 264 VAC
Input Current	0.2 A	0.1 A – 1.0 A
Fuse	5 A, 250 V fast blow glass fuse	

*Overvoltage category III protection

Table 4.17. Stepper motor characteristics.

Maximum Speed	Maximum Force
10 mm/s	45 N

Table 4.18. Pressure characteristics.

Depressurization Target	Working Range	Typical Depressurization Time
40 MPa	40 MPa – 80 MPa	23 s

Chapter 5. Durability Variation Among Medical Gloves Made from Existing and New Elastomers Poses a Risk to Public Health

This chapter is based on the following publication:

Herkins, A., & Cornish, K. (2023). Durability variation among medical gloves made from existing and new elastomers poses a risk to public health. Global Challenges, 7(9). https://doi.org/10.1002/gch2.202300100

This chapter illustrates the use of the Glove Assessment Device described in the previous chapter to conduct a more extensive analysis of glove durability. A wider variety of examination and surgical gloves were sampled from the market for analysis, and a prototype guayule latex surgical glove was also tested. Durability results were compared to those of conventional mechanical testing methods. The impact of adjusting the force setting of the Glove Assessment Device was also analyzed for the reference of future operators. As the first author, I designed the experiments, collected and analyzed the data, and drafted the original manuscript.

5.1. Abstract

Despite being an essential line of defense in preventing the spread of diseases, medical glove durability is neither measured routinely nor has standard specifications. In this study, a new glove durability assessment device was used to objectively compare the durability of gloves made of a variety of elastomers from different manufacturers. Results

were related to several mechanical tests, including stress relaxation, tensile and tear tests. Overall, natural latex gloves far outperformed those made of synthetic elastomers, and there was great disparity among the different brands of nitrile gloves, some of which did not meet required nitrile glove performance requirements.

The study includes prototype gloves made from guayule latex, a domestic source of alternative natural rubber latex, currently under commercial development. The guayule gloves outperformed all other gloves tested, including those made from *Hevea* latex, without posing allergy risks. Mechanical analysis demonstrated that the guayule gloves were as strong as the best alternatives, were softer and more elastic, had better tear strength, and had such low stress relaxation that they cause very little hand fatigue during use. Guayule latex can address the need for domestic production of gloves to resolve supply chain and quality issues and encourage a shift back to natural latex gloves, which would significantly diversify the natural rubber supply.

5.2. Introduction

Healthcare workers rely on medical gloves to protect them and their patients against illness-inducing pathogens such as bacteria and viruses as well as patient contamination with dangerous drugs like fentanyl (Greenawald et al., 2020). Medical gloves provide a physical barrier against blood and other bodily fluids, which may contain these harmful pathogens. Unfortunately, many of these gloves may actually be providing a false sense of security due to lax manufacturing standards and inadequate inspection rates. One study found a 33% leak rate (n = 679) among post-use latex surgical

gloves and a 5.5% defect rate among unused latex surgical gloves, which exceeds the allowable FDA defect rate of 1.5% (Albin et al., 1992).

While the American Society for Testing and Materials (ASTM) does provide general standards for surgical and examination gloves, it does not provide a standard for glove durability once the gloves are removed from their packaging and donned. ASTM's water inflation test for the detection of holes in medical gloves, usually used to test samples of gloves before they are packaged, can be used to check gloves after they have been worn, but this is not useful as a durability measure without a large amount of use data (ASTM International 2019a, 2019b, 2019c). Additionally, ASTM's minimum physical requirements for synthetic gloves such as nitrile, PVC, and polychloride were lowered from the general standards for examination gloves due to the underperformance of these materials. Without a durability standard, some glove manufacturers may produce low quality, easily damaged gloves in order to maximize profits.

Previous studies have demonstrated that glove durability also depends heavily on the material and composition (such as filler loading) of the glove, with natural latex outperforming synthetic materials (Bardorf et al., 2016; Michel & Cornish, 2015; Rego & Roley, 1999; Thomas et al., 2011). Natural latex gloves are also more elastic, softer, equally as strong as premium synthetics, and have lower stress relaxation, allowing extended use without significant hand fatigue. However, the widespread occurrence in the 1990's of life-threatening Type I latex allergies, caused by high levels of soluble proteins in gloves not properly washed during manufacture, led to a shift away from natural latex gloves to petroleum-derived synthetic gloves. Today, about 62.5% of the

global medical glove market is synthetic(*Global Disposable Medical Gloves Market Report, 2030*). The poorer performance of synthetic gloves forced the FDA to approve such gloves for sale under the premise that any glove is better than no glove to control HIV/AIDS transmission. These gloves could not meet the ASTM standards for natural latex gloves, and ASTM established lower standards for the synthetics to accommodate the FDA (ASTM International 2019a, 2019b).

Glove durability also reflects the ability of the specific manufacturer, meaning that two gloves of the same material and specification can have vastly different mechanical and in-use performance (Bardorf et al., 2016; Thomas et al., 2011) This large variation in glove quality combined with the lack of an ASTM durability standard led to the invention of a glove durability assessment device (Venturini et al., 2022). The device works by creating a vacuum within the base of a prosthetic hand, upon which a glove is donned, and repeatedly moving a sandpaper-covered roller into contact with the fingertips of the hand, which are made of porous mufflers (Venturini et al., 2022). The durability of the glove is quantified based on the number of sandpaper touches the glove withstands before perforating.

This study compares the relative durability of dry examination and surgeon's gloves made from a variety of elastomeric materials, both natural and synthetic, and by different manufacturers. Prototype surgical gloves made from guayule latex were also included. This new material is under commercial development and so was assessed in parallel with the existing glove materials. Our hypothesis was as follows:

1. The average number of sandpaper touches would be lower for gloves tested on the New Glove Assessment Device than the Capstone Glove Assessment Device.
2. Gloves made of natural latex would be soft, stretchier, and more durable than synthetic gloves.
3. Thicker gloves would be more durable than thinner gloves of the same type.
4. The greater the force setting on the New Glove Assessment Device, the fewer sandpaper touches would be required for a glove to perforate.

5.3. Durability Testing Devices

5.3.1. Capstone Glove Assessment Device (C-GAD)

The original iteration of the glove durability assessment device (C-GAD) was created by senior engineering students at the Ohio State University as part of a capstone design project (Venturini et al., 2022). The main drawback of the C-GAD was that the gloves needed to be visually inspected for perforations while the testing device was stopped, which reduced the precision of results to a minimum inspection interval of 5 seconds (Venturini et al., 2022).

5.3.2. New Glove Assessment Device (N-GAD)

The new glove assessment device (N-GAD) was built to improve upon the C-GAD prototype. It is fully mechanized and automatically detects glove breakage immediately, eliminating the need for visual glove inspection. It is also more controllable, with adjustable settings for roller force and motor speed (touch interval), and has a liquid spray system that allows the user to simulate glove use in wet

environments, although this function was not used in the current study (Venturini et al., 2022).

5.4. Materials and Methods

5.4.1. Glove Durability Tests

A variety of gloves were tested in random order on the N-GAD and the C-GAD, and the results were compared. Both surgical and examination gloves were tested, and the glove materials included natural latex, nitrile, polychloroprene, and polyisoprene. To ensure that the results from each glove tester were comparable, both the number and size of each glove type were kept as consistent as possible between the C-GAD and the N-GAD. It should be noted, however, that glove sizes 6 and 6.5 were too small for the prosthetic hand of the N-GAD, so size 7 was used instead. In addition, while the N-GAD was capable of testing both left and right-handed gloves due to the lack of a thumb on the prosthetic hand, the C-GAD was only capable of testing right-handed gloves. Therefore, due to limited availability of larger-sized polychloroprene gloves, sizes 6, 6.5, and 7 were tested using the C-GAD. For both devices, the default microcontroller settings were used to maintain consistency, including an applied force of 15 N and a motor speed of 3.5 mm/s which supports a touching interval of approximated one touch every 6 seconds. The data collected included the time and number of touches until the glove was punctured.

A larger array of gloves then was tested using the N-GAD in order to compare glove materials and brands. The tested gloves included three types of nitrile gloves (Vglove, Restore Touch, and U.S. Medical Glove; all examination gloves), three types of

Hevea latex gloves (Aloe Touch; examination, Triumph Green; surgical, and Triumph Micro; surgical), one type of polyisoprene glove (Sensicare Micro; surgical), one type of polychloroprene glove (Neolon; surgical), one type of polyvinyl chloride glove (Safeko; examination), and one type of guayule latex glove (EnergyEne; surgical). Examination gloves were sizes medium and large, and surgical gloves were sizes 7 and 8. Depending on availability, either three or five replicate gloves were tested from each type. The time and number of touches until the glove was punctured were recorded, as well as the force used.

5.4.2. Thickness Measurements

Four thickness measurements were collected for three gloves of each type, using an electron caliper: three around the cuff and one at the fingertip. The third (ring) finger was selected for fingertip thickness sampling because it is one of the fingers that comes into contact with the rough surface of the drum on the N-GAD. Fingertip thickness measurements were performed after durability testing because these measurements required the removal of the glove finger, effectively destroying the glove.

5.4.3. Force Tests

Three samples of nitrile, *Hevea* latex, and guayule latex examination gloves were tested at forces of 8, 10, 13, 15, and 20 N to determine the correlation between the force applied by the N-GAD and the number of touches until the glove failed and validate the use of higher forces for thicker gloves. The most durable gloves were not tested at the lowest force levels, however, due to extremely long wait times until glove breakage.

5.4.4. Guayule Gloves

Guayule gloves were made one at a time, as described for guayule radiation attenuation gloves except that no Bi_2O_3 filler was added (Ramirez Cadavid et al., 2022). The same xanthate-based curing package was used which prevents the contact reactions and Type IV skin allergies often caused by the traditional carbamate, thiuram and thiazole chemical crosslinking accelerators (Virdi et al., 2019). Thus, guayule latex gloves are circumallergenic because they avoid Type I systemic reactions and Type IV and contact allergic reactions.

5.4.5. Mechanical Tests

Tensile measurements according to ASTM D412 were used compared the performance of guayule gloves and gloves made tropical natural latex, nitrile, and polyvinyl chloride (ASTM International 2021). Five dumbbells were cut using Die D from glove films (CCSI, Akron, OH, USA). Sample tensile properties were determined using a tensiometer (model 3366, Instron, Norwood, MA, USA) with a 50 N static load cell (model 2530-50N, Instron), equipped with a contact extensometer (model 3800, Epsilon Tech. Corp., Jackson, WY, USA). Tensile strength (stress), elongation to break, and modulus at 500% strain) were derived using Bluehill v. 2.26 software (Instron, Norwood, MA, USA). Stress relaxation was measured by elongating a sample to the desired strain (100%, 300%, or 500%), and recording the decrease in stress over a 15-minute period. Tear strength was determined according to ASTM D624 using notched dumbbells and the tensiometer described above (ASTM International 2020a). Tear

strength was measured by pulling the notched test sample apart and measuring the minimum amount of force required to initiate the tear.

5.4.6. Statistical Analysis

One- and two-way analyses of variance ($\alpha = 0.05$) were performed using the statistical software JMP 14. Except for the direct comparison on the C-GAD and N-GAD, extreme outliers were removed from the data to ensure that the mean value accurately represented the data set. A student's t-test was also performed on individual data gathered using the N-GAD so that specific glove-to-glove variability could be identified.

5.5. Results

5.5.1. N-GAD and C-GAD Comparison

Although the collected data included both time to failure and number of sandpaper touches to failure, the statistical analyses focused only on the number of touches because the time interval between touches occasionally varied. The N-GAD was programmed to maintain a pressure differential by repeatedly de-pressurizing at random intervals throughout the test while the timer remained on, and so the time and number of touches did not directly correspond with one another.

The number of touches to failure was similar with both devices except for the polyisoprene surgical glove (Sensicare Micro) (Figure 5.1.). The higher C-GAD mean is likely due to the lower accuracy of manual glove inspection because very small perforations are often difficult to see and may be missed, artificially increasing the

overall average number of touches to obvious failure. The N-GAD eliminates human error from the glove durability testing process.

No significant difference was observed between the results from the two devices (Table 5.1.) and there was no interaction between glove type and device. However, the different gloves did have significantly different durability ($P < 0.0001$). The variability within the replicates was very high. Surgeon's gloves "latex #3" and the polyisoprene version, had gloves which were among the most and least durable of those tested.

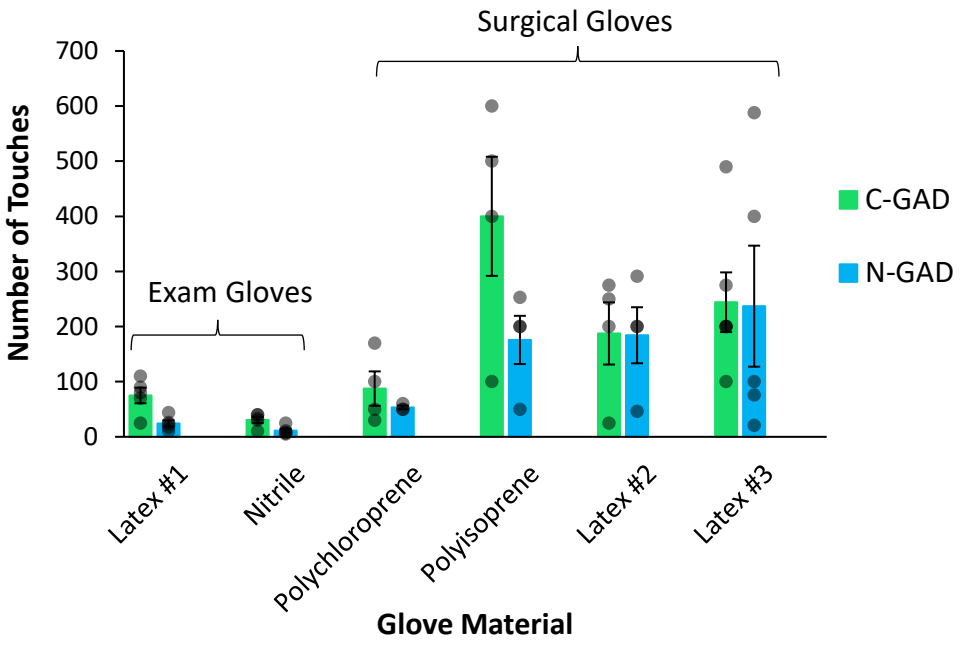


Figure 5.1. Comparison of glove durability assessed by two durability testing devices. Each value is the means of 3 to 5 samples ± standard error. The individual points are also plotted (gray circles).

Table 5.1. Two-way analysis of variance comparing glove failure rates on the C-GAD and N-GAD. Note that $\alpha = 0.05$.

Source of Variation	Degrees of Freedom	Sum of Squares	F Ratio	Probability
Glove Brand	5	558,806	8.115	< 0.0001
Device	1	41,798	3.035	0.089
Glove Brand x Device	5	72,774	1.057	0.398

5.5.2. Durability of a Broad Range of Gloves

When the N-GAD was used to quantify the durability of a wide variety of glove materials and brands (Figure 5.2.), a one-way analysis of variance ($\alpha = 0.05$) indicated that their durability significantly differed ($P < 0.001$) (Table 5.2.). Student's t-tests determined statistically significant glove-to-glove differences and indicated that the EnergyEne brand prototype guayule latex gloves were significantly more durable than all other gloves tested (Table 5.3., Figure 5.2.). The two glove brands with the lowest averages, Vglove and Safeko, were statistically different than the four glove brands with the highest averages, EnergyEne, Sensicare Micro, Triumph Green, and U.S. Medical Glove (Table 5.3.).

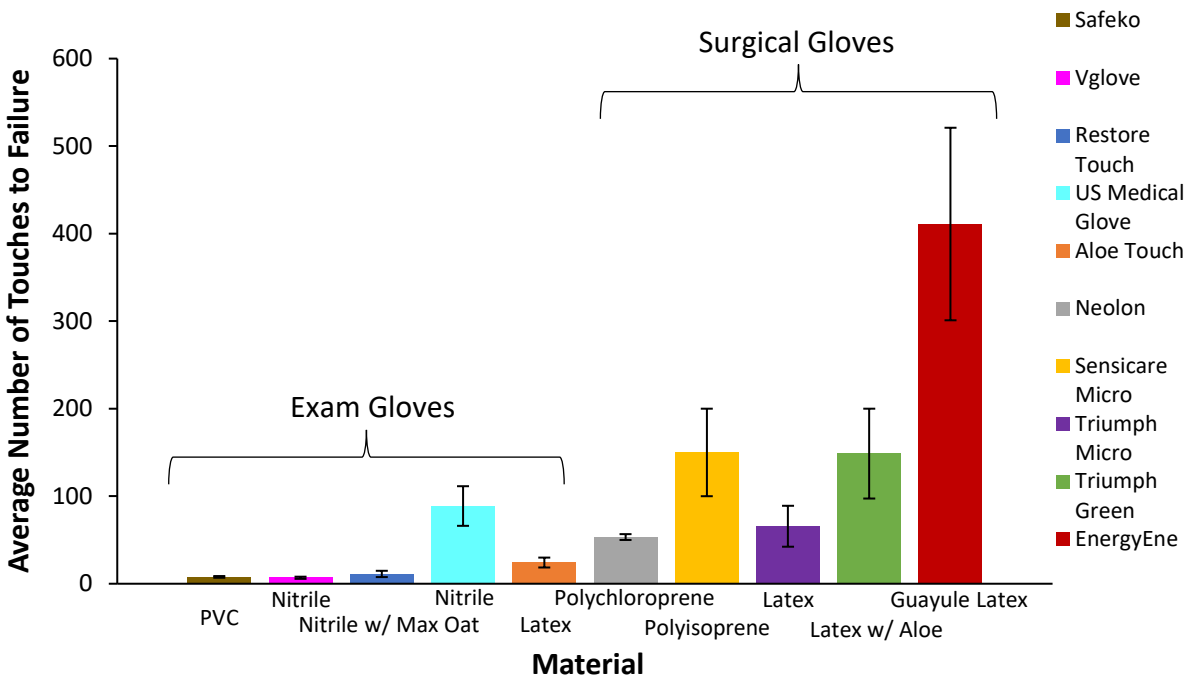


Figure 5.2. Average number of sandpaper touches to glove failure ± standard error.

Table 5.2. One-way analysis of variance comparing glove failure rates for various glove types using the N-GAD. Note that $\alpha = 0.05$.

Source of Variation	Degrees of Freedom	Sum of Squares	Mean Square	F Ratio	Probability
Glove Brand	9	452746	50305	12.8	<0.0001
Error	30	117934	3931	-	-
Total	39	570680	-	-	-

The durability variability within individual glove types is also apparent between gloves manufactured by different companies from the same material (Figure 5.2.). For example, among the three nitrile examination glove brands tested only the US Medical

Glove product was reasonably durable and far outlasted the other nitrile gloves as well as the thin Aloe Touch natural latex glove. The Vglove was the worst glove tested, and user experience (Cornish laboratory) of how quickly this glove fails when donned (within a few seconds) matches the test data.

Table 5.3. Student's t-test comparing glove failure rates for various glove types using the N-GAD. Different letters indicate significantly different durability. Examination gloves are the mean 5 samples, and surgical gloves are the mean of 3 samples.

Connecting Letters Report				
Brand				Mean
EnergyEne	A			411.00
Sensicare Micro		B		150.00
Triumph Green		B		148.67
U.S. Medical Glove		B	C	88.80
Triumph Micro		B	C	D	65.67
Neolon		B	C	D	53.33
Aloe Touch			C	D	24.20
Restore Touch			C	D	11.20
Safeko				D	7.80
Vglove				D	6.80

5.5.3. Glove Thickness and Durability

Gloves tend to be thicker at the fingertips than at the cuff, and thickness varies depending on material and manufacturer (Figure 5.3.). The same data are represented in the form of the average ratio of cuff thickness to fingertip thickness (Table 5.4.), and the data are also ranked in numerical order. In general, thicker gloves are more durable, regardless of the material. Thicker gloves also need more abrasive contact before they puncture (Figure 5.4.), meaning that they are a more effective barrier against harmful pathogens.

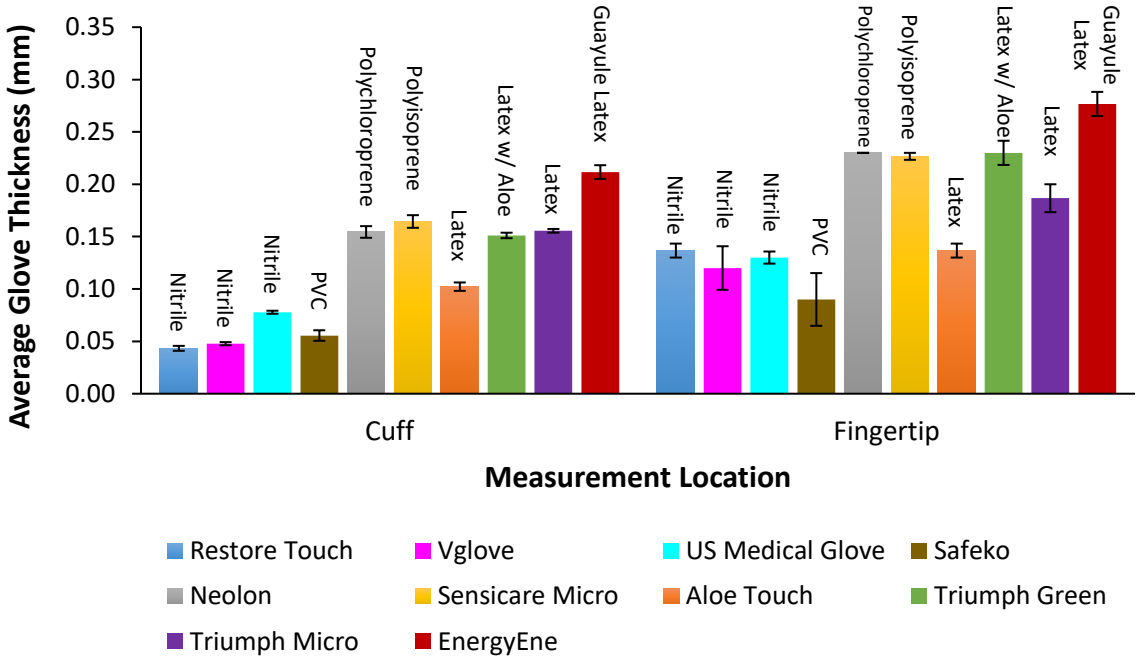


Figure 5.3. Average thickness of various glove types at the cuff and fingertip ± standard error.

Table 5.4. Average ratio of cuff thickness to fingertip thickness based on three samples of each glove variety ± standard error. Data are ranked from lowest ratio to highest ratio. Neolon brand does not have a standard error ratio because the standard error for the fingertip measurements was 0.

Brand	Average Ratio of Cuff Thickness to Fingertip Thickness
Vglove	0.42 ± 0.07
Restore Touch	0.51 ± 0.35
US Medical Glove	0.60 ± 0.25
EnergyEne	0.65 + 0.57
Triumph Green	0.66 ± 0.23
Neolon	0.67 ± 0.00
Safeko	0.70 ± 0.20
Sensicare Micro	0.72 ± 1.81
Aloe Touch	0.75 ± 0.60
Triumph Micro	0.84 ± 0.13

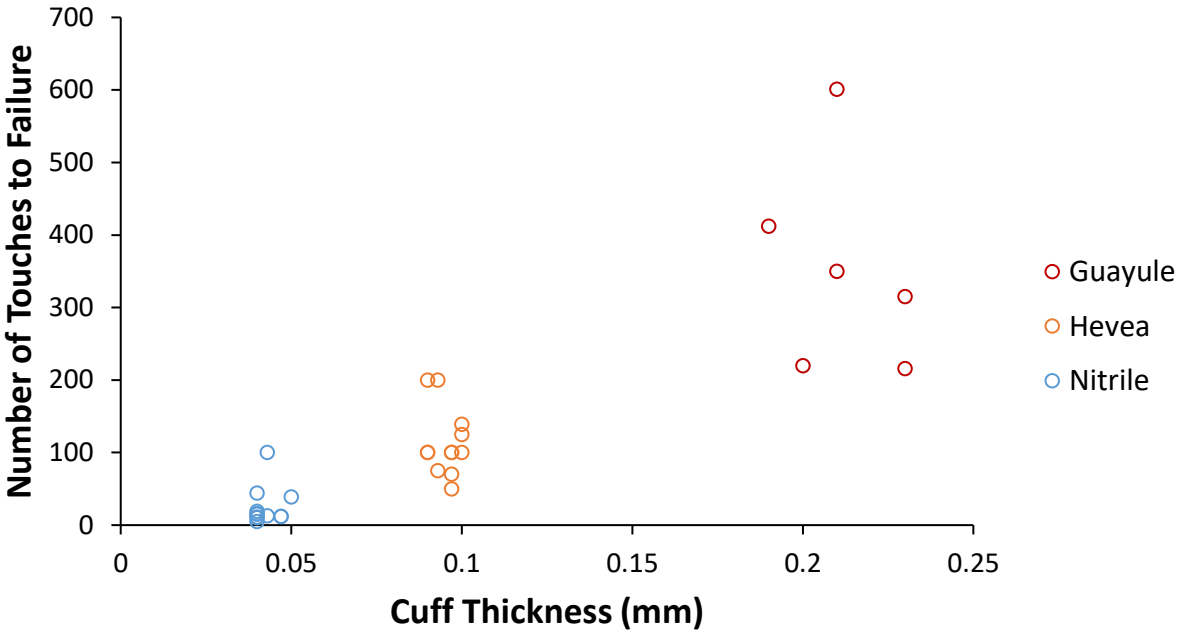


Figure 5.4. Number of touches to failure vs. glove cuff thickness for *Hevea* latex, synthetic nitrile, and guayule latex.

The large variation in the number of touches to failure for guayule latex gloves is due to each guayule glove being individually dipped. Also, different dwell times were used to change thickness. These result in less-consistent durability between these prototype gloves than mass-manufactured gloves.

5.5.4. Force Testing

One of the adjustable settings on the N-GAD is the force the sandpaper roller applies to the prosthetic hand (Venturini et al., 2022). Altering this setting dramatically changes the number of touches to glove failure. However, durable gloves may take too long to test using the force required for assessing flimsy gloves (Figure 5.5.). Identifying

trends in break times vs. applied force provides a point of reference for testing gloves on the N-GAD.

It should be noted that not all glove types were tested at all forces, as the number of touches to failure increased to rather extreme time periods as the force decreased (consecutive touches are approximately 6 seconds apart) (Figure 5.5.). Guayule latex gloves were not tested at forces lower than 15 N due to extremely long times until failure (over an hour per glove at a minimum). *Hevea* latex gloves were also not tested below 10 N for the same reason, with break times reaching over 26 minutes per glove.

The separation of relative durability of the different glove materials was maintained at the different forces (Figure 5.5.) and the natural latex gloves exhibited a negative linear relationship of force and number of touches to break. Restore Touch nitrile gloves had two distinct trendlines: the one with a slope of -0.2 is relevant to glove testing. The second plottable trend line with a slope of -0.0009 indicates that these gloves basically could not withstand touches with any force over 13 N. Plotting such trends will aid with future N-GAD studies in which the force must be adjusted from its default setting, and also provides context for the data collected in this study at the default force of 15 N.

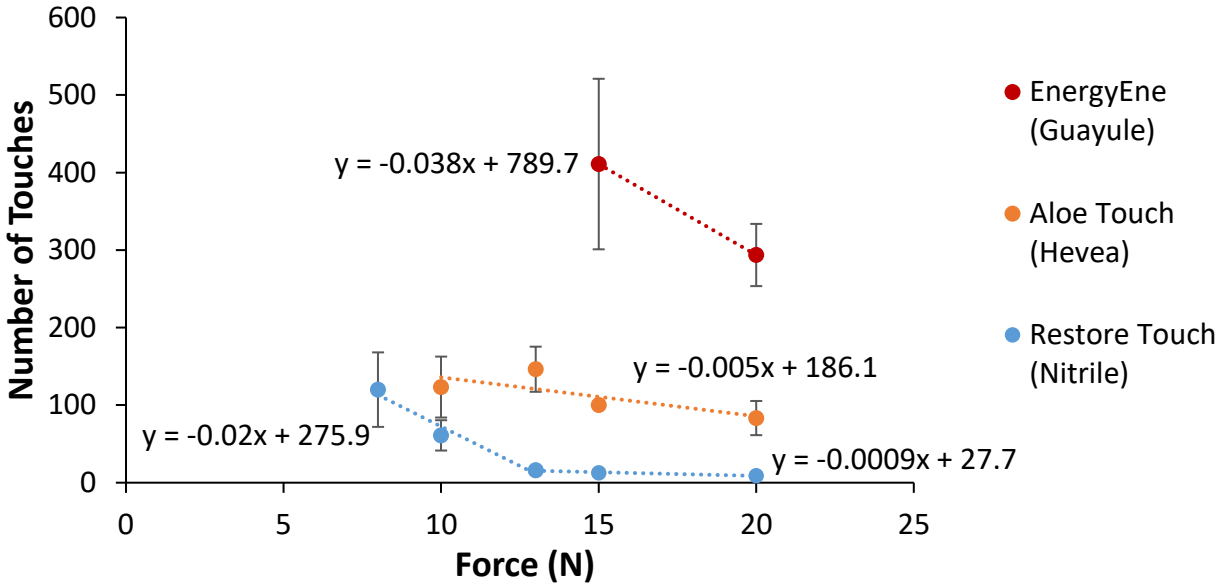


Figure 5.5. Number of touches to glove failure vs. applied force ± standard error for *Hevea* latex, synthetic nitrile latex with colloidal oatmeal, and guayule latex. Each value is the mean of 3 gloves ± standard error. Note: some error bars are smaller than the symbol height.

The unit for applied force used in this study is Newtons rather than Pascals because Newtons are a measure of force that is independent of thickness. A Pascal is derived by dividing the force in Newtons by the area of the test sample, usually in square meters. Since glove thicknesses vary among materials and brands (Figure 5.3.), Newtons were the more appropriate unit of force for the N-GAD. Although some ASTM glove standards include Newtons, most use Pascals, and reported forces are highly affected by film thickness.

5.5.5. Material Properties

Natural latex gloves are much more comfortable to the wearer due to their superior mechanical properties. As shown by the stress strain curve (Figure 5.6.), the natural latex gloves, *Hevea* and guayule, are more elastic than synthetic gloves (PVC and a high-quality purple nitrile glove), with guayule being the most stretchable. The point at which the plots end is where the testing dumbbell broke in two. The nitrile and guayule glove films were of similar strength, and this is generally the case when high quality nitrile gloves are tested. The modulus (effectively, softness) difference is apparent in the vertical plain of these curves: the lower the number, the greater the softness.

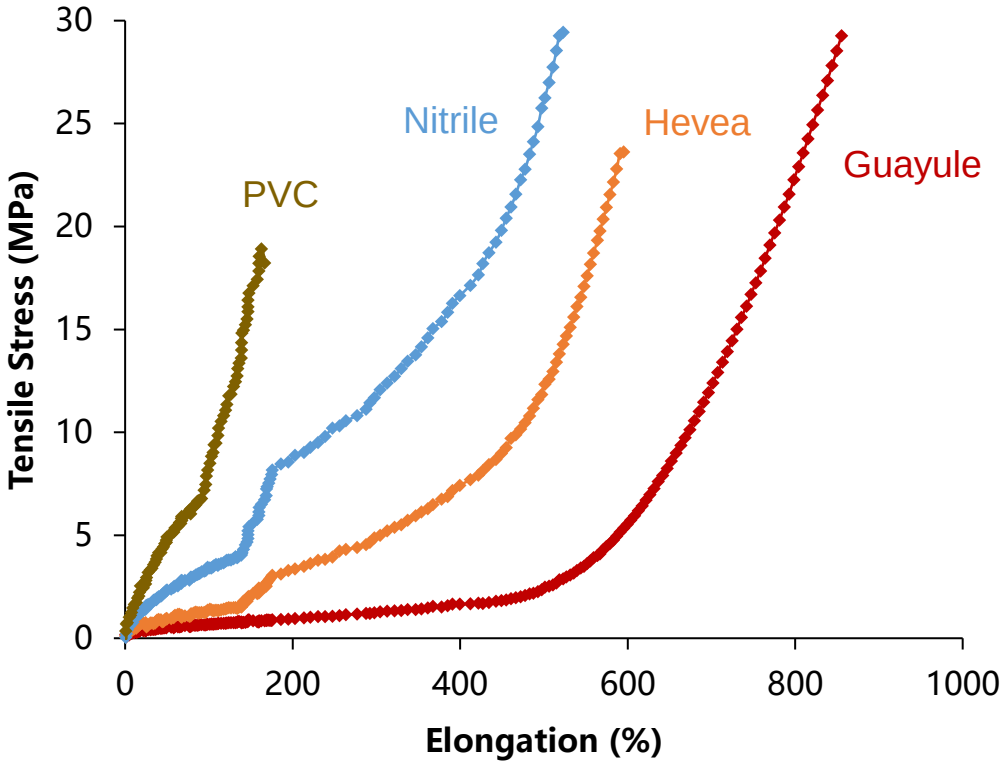


Figure 5.6. Tensile stress vs. percent elongation for PVC, nitrile, Hevea, and guayule gloves.

The stress relaxation force reflects the resistance of the glove to deformation (Figure 5.7.). Thus, the nitrile glove, when first donned, is very stiff and requires substantial hand energy for several minutes as the glove warms and softens. It remains more resistant to hand movement than the two natural latex gloves. Neither of these changes much over time. The energy required to stretch guayule latex films is very low compared to other materials (Figure 5.7.). This makes for easier donning and more comfortable wear, and it fits like a “second skin".

When stress relaxation was determined at three elongations to compare PVC, nitrile, *Hevea*, and guayule, the synthetic gloves were much stiffer than the natural gloves

during the first few minutes of testing (Figure 5.8.). Although PVC and nitrile substantially softened during repeated manipulation, PVC remained the stiffest glove throughout the trial, followed by nitrile, *Hevea,* then guayule. PVC was able to reach 300% elongation during the stress relaxation tests but reached less than 200% elongation in the tensile stress test. This reflects the presence of manufacturing inconsistencies among the PVC glove samples (Figure 5.6.).

Natural latex gloves were more tear resistant than nitrile gloves and other synthetics (Figure 5.9.). This is because natural rubber forms crystallites when the material is stretched and the polymers align. This phenomenon, stress-strain crystallization, is a main cause of the better performance of natural rubber than synthetic elastomers in many applications (Ikeda et al., 2016; Junkong, Cornish, & Ikeda, 2017; Junkong et al., 2019; Junkong, Ohashi, et al., 2017). When material failure begins, cracks do not propagate beyond the first crystallite it encounters. Thus, crystallites block crack propagation and inhibit tearing (Zhang et al., 2009).

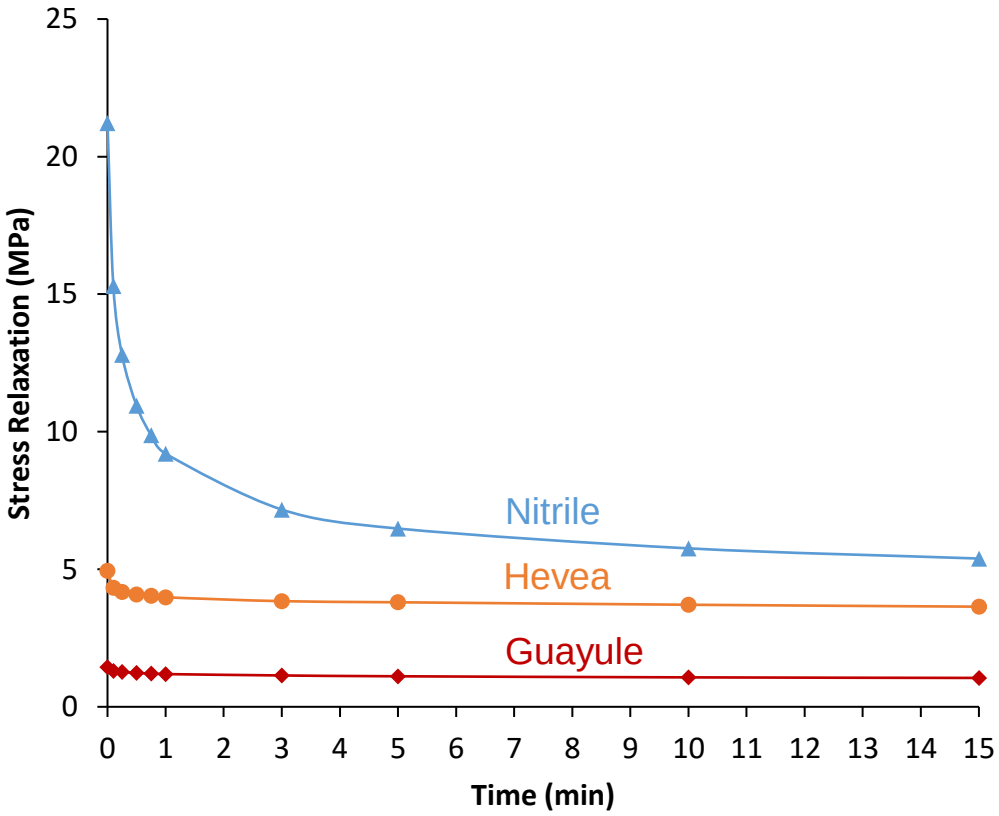


Figure 5.7. Stress relaxation over a time period of 15 minutes for nitrile, *Hevea*, and guayule latex gloves.

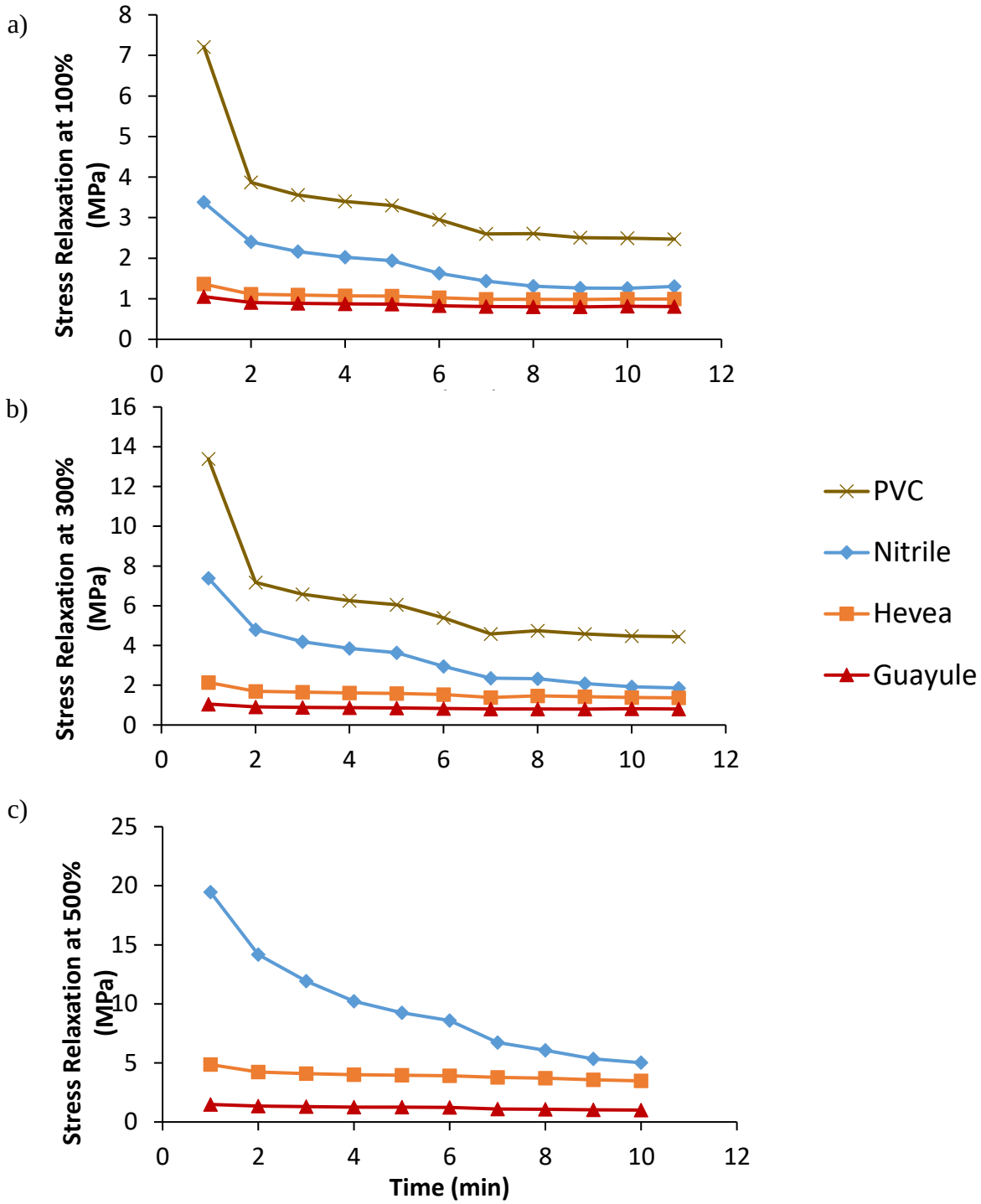


Figure 5.8. Stress relaxation for PVC, nitrile, *Hevea*, and guayule latex gloves at a) 100% elongation, b) 300% elongation, and c) 500% elongation. PVC is not included in the 500% elongation graph because it was unable to elongate to 500% without breaking.

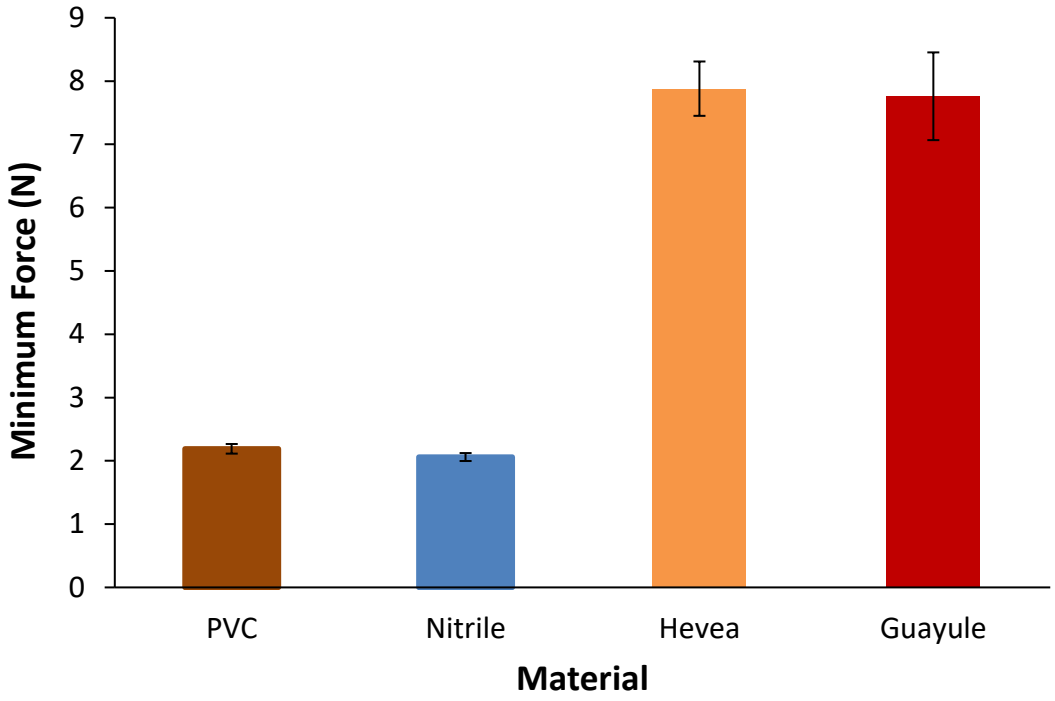


Figure 5.9. Average minimum force required to initiate a tear, in Newtons ± standard error for PVC, nitrile, *Hevea* and guayule examination gloves.

5.5.6. ASTM Standards

ASTM provides standard specifications for surgical gloves as well as examination gloves (ASTM International 2019a, 2019b). However, depending on the specific material, these minimum physical requirements may actually be much lower than the general standards for surgical and examination gloves. For instance, synthetic gloves such as polyvinyl chloride, polychloroprene, and nitrile that are typically used as examination gloves all have minimum tensile strength and ultimate elongation requirements less than that of the standard for general Type II unaged examination gloves (Table 5.5.) (ASTM International 2019d, 2019e, 2019f) Polychloroprene and nitrile

gloves are also held to a lower standard in terms of thickness, with their minimum requirement of 0.05 mm being less than the general exam glove minimum requirement of 0.08 mm (Table 5.5.).

Table 5.5. ASTM physical requirements for examination and surgical gloves versus specific glove materials. Type I gloves are composed of natural rubber latex, and Type II gloves are composed of rubber cement or synthetic rubber latex.

				Before Aging		After Accelerated Aging	
Standard Specification Title	Designation	Type	Thickness (mm)	Tensile Strength (MPa minimum)	Ultimate Elongation (% minimum)	Tensile Strength (MPa minimum)	Ultimate Elongation (% minimum)
Rubber Examination Gloves	D3578-19	I	0.08	18	650	14	500
		II	0.08	14	650	14	500
Rubber Surgical Gloves	D3577-19	I	0.10	24	750	18	560
		II	0.10	17	650	12	490
Poly(vinyl chloride) Gloves for Medical Application	D5250-19	II	0.08	11	300	-	-
Nitrile Examination Gloves for Medical Application	D6319-19	II	0.05	14	500	14	400
Polychloroprene Examination Gloves for Medical Application	D6977-19	II	0.05	14	500	14	400

5.6. Discussion

Our data prove that, in general, natural latex gloves are more durable than synthetic ones and so provide a more effective barrier against pathogens. Their mechanical properties also make them a more comfortable and less tiring glove to wear (Mylon et al., 2014). For synthetic PVC and nitrile gloves, the more movements the wearer makes, the more resistance the glove poses to such movements, unlike guayule which poses little resistance (Figure 5.6.).

Among the surgical gloves, natural latices tended to outperform synthetics. The poorer durability of the natural latex Triumph Micro surgical glove compared to the Triumph Green one (Figure 5.2.) was not due to a thickness difference (Figure 5.3.), so probably reflects differences in the manufacturing protocols used to make them. This raises a serious concern about the quality control of their manufacturing processes because every user expects reproducible performance from different examples of a specific glove and brand.

The large disparity in the average number of touches to failure for the three nitrile glove brands (6.8 for Vglove, 11.2 for Restore Touch, and 88.8 for U.S. Medical Glove) indicates that some imported gloves are seriously substandard. These gloves have similar thickness (Figure 5.3.), so Vglove and Restore Touch either have serious manufacturing issues, or they are not made of 100% nitrile, or have a high loading of diluent filler(s). In addition, the average cuff thicknesses of these two glove types fell below the minimum ASTM required thickness of 0.05 mm for unaged nitrile gloves (Table 6.5.) (ASTM International 2019e). Similarly, the Safeko brand PVC gloves, which are also synthetic,

failed to meet the ASTM minimum ultimate elongation of 300% for unaged PVC gloves (Table 5.5.), breaking below 200% (Figure 5.6.). This raises serious concerns over the safety of these medical gloves, which claim to meet ASTM standards. When healthcare workers use gloves, they rely on them to act as physical barriers against disease transmission. Cheap synthetic gloves are cheap for a reason, and it is clearly important to avoid purchasing them even when they are dumped on the U.S. market. Saving a few dollars by acquiring unsafe gloves can cost people their health and even their lives. The authors encourage all glove manufacturers to create high-quality products that will protect the public from exposure to harmful pathogens.

From the thickness tests, it may initially appear that the solution to the issue of glove durability is to create thicker gloves. However, thicker gloves are also stiffer and reduce the tactile sensitivity of the wearer's hands. Both of these qualities are undesirable for medical gloves because dexterity is essential for delicate surgeries and other medical procedures, and thicker gloves may hinder the performance of the healthcare provider and lead to undesirable patient outcomes.

The lack of control U.S. users have over glove quality, and the disruption of supply chains experienced during the COVID-19 pandemic, have led to onshoring of nitrile glove manufacturing, and increasing emphasis on raw material manufacture, including production of natural rubber and natural rubber latex within our borders (Bown, 2022).

It is worth noting that properly leached (washed), polymer coated, unpowdered natural latex gloves made from latex tapped from tropical rubber trees can be used safely

by people who do not already have Type I latex allergy (Cornish, 2012). Since most natural latex gloves imported into the U.S. market (at least before the COVID-19 pandemic), are properly leached and contain very little soluble protein (< 50 µg/g, see ASTM D6699) it seems more likely that a user would contract a disease through synthetic glove breakage than have a dangerous anaphylactic reaction to residual proteins in a natural latex glove (ASTM International 2016). However, although data is amassing proving that COVID-19 has impelled the manufacture and import of cheap, poor quality synthetic gloves there is, as yet, no information on whether any natural latex glove manufacturers have chosen to lower their costs by taking their leaching step out again. If any take this irresponsible approach, a new wave of Type I latex allergy sensitization would occur. Some dental dam manufacturers do not leach their natural latex dams, so this concern is not without precedence (Cornish et al., 2019). Normal detergents in hot or cold water do not effectively extract entrained proteins remaining in un-leached, fully cured natural latex films, but human fluids can do this during medical or dental procedures. Leaching is only effective during manufacture when applied to partially cured products.

Because the findings of this study are imperative to the health and safety of healthcare works, a table summarizing the authors' recommendations has been included (Table 5.6.).

Table 5.6. Author recommendations for healthcare workers. The quality of gloves was ranked using the following scale: Excellent, Good, Fair, Poor, Very Poor. Please note that examination and surgical gloves are *not* directly comparable in terms of quality rating.

Brand	Material	Intended Use	Quality Rating
Vglove	Nitrile	Examination	Very Poor
Restore Touch	Nitrile	Examination	Poor
US Medical Glove	Nitrile	Examination	Excellent
Safeko	PVC	Examination	Very Poor
Aloe Touch	*Hevea* Latex	Examination	Poor
Triumph Green	*Hevea* Latex	Surgical	Good
Triumph Micro	*Hevea* Latex	Surgical	Fair
Neolon	Polychloroprene	Surgical	Fair
Sensicare Micro	Polyisoprene	Surgical	Good
EnergyEne	Guayule Latex	Surgical	Excellent

5.7. Conclusions

Examination and surgeon's gloves are extremely variable in durability, when tested dry and in air, even within a specific elastomeric material, indicating fundamental flaws in manufacturing protocols, quality control, and inspection rates. Unexpectedly flimsy gloves pose a threat to the health and wellbeing of all wearers, their patients, and their colleagues. Also, medical gloves are not solely used in dry environments and

additional research will include testing durability under wet conditions, such as in water, ethanol, and phosphate buffered saline to simulate more realistic user environments (Michel & Cornish, 2015). Durability under these conditions may be poorer than in air. It will be important to determine any correlation between wet and dry glove durability before an ASTM durability standard can be proposed. Overall, gloves made from guayule latex, an allergy-safe domestic source of alternative natural rubber latex were more durable than the other gloves tested, including those made from *Hevea* latex (Cornish, 2012). Guayule gloves (and condoms) have previously been demonstrated to be effective barriers against viruses, including the φX174 virus, which, with a diameter of 27 nm, is smaller than the smallest known human pathogenic virus (Cornish & Lytle, 1999). This indicates that guayule latex gloves are also effective barriers against larger pathogenic viruses.

Guayule latex is as strong as nitrile and as tear resistant as *Hevea* latex while also having a more comfortable, lightweight feel that allows the user to almost forget they are wearing gloves. Compared to other products such as the FlexiPalm, guayule latex gloves have similar features such as an inconspicuous and comfortable design, but guayule gloves have the added benefit of providing a barrier for the entire hand, rather than just the palm (Tan et al., 2023). Although the palm may be the main transmission point for pathogens, a hand that is fully covered is fully protected from transmitting or being contaminated by harmful bacteria and viruses. Guayule latex gloves are currently not produced on a commercial scale. However, examination, surgical, and radiation

attenuation guayule latex gloves have been prototyped by multiple companies, tested by consumer groups, and consistently judged best in class.

Guayule latex can address the need for domestic production of gloves to resolve supply chain and quality issues. A shift back from synthetic latices, which are made from petroleum, to natural latices, which are made from plants, would greatly reduce the carbon footprint of the medical glove industry as a whole and biologically and geographically diversify the natural rubber supply.

5.8. Acknowledgements

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Chapter 6. Nitrile Glove Composition and Performance – Substandard Properties and Inaccurate Packaging Information

This chapter is based on the following manuscript:

Herkins, A., Dey, S., Conroy, D., & Cornish, K. (2024). Nitrile Glove Composition and Performance – Substandard Properties and Inaccurate Packaging Information. PLOS One. Under Review. (Peer Reviewed)

This chapter builds off the findings from the Chapter 5. The three brands of nitrile gloves tested in the previous chapter did not have the same durability performances despite being made of the same material. This study investigates whether these underperforming nitrile gloves were truly made of nitrile as advertised, or if they were adulterated with a cheaper polymer or filler. As the first author, I assisted in experimental design and data collection and was primarily responsible for data analysis and drafting the manuscript.

6.1. Abstract

The durability and mechanical properties of synthetic medical gloves, such as those made from nitrile, vary drastically depending on the manufacturer. This study reports the chemical composition of several brands of nitrile gloves via FTIR and solid-state NMR analysis and relates composition to glove durability (found via GAD), mechanical performance (found via Instron), and whether the gloves meet or fail ASTM

International standards. Out of the four nitrile examination glove brands tested, American Nitrile Slate brand had superior durability results and was found to be made of acrylonitrile butadiene rubber, as expected. The U.S. Medical glove brand, which was also found to be pure nitrile, had the superior tensile results, consistently reaching over 800% elongation before breaking. Although Restore Touch brand exam gloves were made of nitrile, they exhibited substandard tensile strength and durability due to the thinness of the glove, which barely met the ASTM minimum thickness value. The Vglove brand glove had the overall worst mechanical properties, did not meet ASTM requirements, and had an NMR spectrum consistent with that of a polyvinyl chloride glove, rather than nitrile. Gloves that fail to meet the minimum performance requirements should not be used for medical purposes to protect the health and safety of consumers.

6.2. Introduction

Protective gloves are a first line of defense for healthcare workers and their patients, protecting against the transmission of pathogens and toxins. Acrylonitrile butadiene rubber (NBR) is a petroleum-based synthetic polymer that is widely used to manufacture examination gloves. Although not as durable or as comfortable as natural latex gloves (Bardorf et al., 2016; Herkins & Cornish, 2023; Michel & Cornish, 2016; Rego & Roley, 1999; Thomas et al., 2011) nitrile and other synthetic gloves do not induce Type I latex allergic reactions, as may occur when using improperly leached natural latex protects (Cornish, 2012). The COVID-19 pandemic caused an unprecedented surge in demand for nitrile gloves. Consequently, low inspection rates of

these gloves resulted in the U.S. market being flooded with poorly made products in recent years (*Global Disposable Medical Gloves Market Report, 2030*).

Previous durability studies have demonstrated that nitrile gloves have vastly different in-use times to failure depending on the manufacturer, and many brands failed to meet the minimum requirements specified by ASTM International (ASTM D-6319) and the U.S. Food and Drug Administration (FDA) (ASTM International 2019b, 2019e; Thomas et al., 2011). This has raised serious concerns as to whether these gloves are simply poorly made, or if the nitrile has been partially or completely substituted by a cheaper, less durable alternative, such as polyvinyl chloride (PVC), or by diluent fillers like calcium carbonate. Even a tear the size of a pinhole can allow pathogenic viruses and bacteria, some of which are deadly, to transfer through the medical glove.

The purpose of this study is to evaluate a range of gloves imported into the United States as nitrile examination, emergency response technician (EMT) and industrial-grade gloves with respect to their polymer composition, durability, and mechanical properties. We hypothesized that Vglove brand nitrile gloves would underperform in tensile and durability tests compared to other nitrile gloves because it is either made entirely of PVC or is a PVC blend.

6.3. Methods

6.3.1. Glove Samples

This study is not intended to survey all brands and manufacturers of nitrile gloves but is an in-depth evaluation of a selection of readily available gloves in use at our

institution. All gloves tested were brand new and unused. The gloves that were tested had no visible holes, tears, or physical defects prior to testing. Four brands of nitrile examination gloves (Restore Touch, U.S. Medical Glove, Vglove, and American Nitrile Slate), two brands of nitrile EMT gloves (Curaplex and Ansell Life Star), and one brand of industrial-grade nitrile gloves (N-Dex Plus) were evaluated. One brand of polyvinyl chloride (PVC) gloves (Safeko) was used as a positive control for FTIR tests. One brand of glove made from natural *Hevea* latex (Aloe Touch) was included in the FTIR testing as an additional reference. A solidified sample of pure nitrile latex was used as a negative control for FTIR tests. All gloves tested were a size large, with the exceptions of Safeko and Aloe Touch brands, which were both size medium. Manufacturer information: Restore Touch (Medline), $0.09/glove, Northfield, IL, USA, U.S. Medical Glove, $ 0.09/glove, Montgomery, IL, USA, American Nitrile Slate, $0.15/glove, Grove City, Ohio, USA, Curaplex, $0.25/glove, Dublin, OH, USA, Ansell Life Star, $0.29/glove, Iselin, NJ, USA, 8005PF N-Dex Plus (Showa Gloves), $0.17/glove, Menlo, GA, USA, Safeko, $0.05/glove, Brooklyn, New York, USA, Aloe Touch (Medline), $0.10/glove, Northfield, IL, USA. Vglove brand does not provide manufacturing information for their gloves, either on their packaging or online.

6.3.2. Durability Tests

Durability testing was performed using the Glove Durability Assessment device (GAD), which was developed to allow the user to objectively compare the durability of medical gloves without the need for manual inspection (Thomas et al., 2011; Venturini et al., 2022). Previous reports refer to this device as the New Glove Durability Assessment

Device (N-GAD). Five trials were performed for each glove brand and type, with the exception of Ansell Life Star brand EMT gloves, for which four trials were performed due to limited quantities available. The 120-grit sandpaper used to create a rough glove contact surface was replaced between each trial. The default settings for roller force (15 N) and speed (3.5 mm/s) were utilized for these durability tests. Following durability testing, the middle finger of each glove was removed, and the thickness of the fingertip (mm) was measured using electronic calipers. The thick N-Dex industrial glove was too stiff to fit onto the mandrel, and so durability could not be assessed.

6.3.3. Tensile Tests

Tensile data were collected according to a modified version of ASTM D412 (ASTM International 2021). Five dumbbells were cut out of the glove samples using Die C (CCSI, Akron, OH, USA). Tensile properties were determined using a tensiometer (model 5542, Instron, Norwood, MA, USA). The thick N-Dex glove (0.39 mm average) usually failed to break during the tensiometery tests, and so was not included in the dataset.

6.3.4. Fourier Transform Infrared Tests (FTIR)

A square-shaped sample with a side length of approximately 12.7 mm was cut from each glove and placed on the crystal. For the solidified pure nitrile, a thin layer was placed so that it completely covered the crystal. The pressure clamp was then used to press the sample. Spectral data were collected using an FTIR spectrometer (model 4500a, Agilent Technologies Inc., Danbury, CT, USA) equipped with a diamond-ATR accessory, ZnSe beamsplitter and DTGS detector. MIR spectra were collected over the

range of 4000-700 cm^{-1} with a resolution of 4 cm^{-1}, and 64 spectra were co-added to improve the signal to noise ratio. The infrared spectra of background and samples were recorded on a personal computer using Agilent MicroLab PC software (Agilent Technologies Inc., Danbury, CT, USA). The device was thoroughly cleansed with ethanol and wiped clean between samples to prevent cross contamination.

6.3.5. Solid State Nuclear Magnetic Resonance Tests (NMR)

Glove samples were cut up and packed into 3.2 mm zirconium rotors and spun at 10 kHz MAS at 300 K. An aqueous dispersion of butadiene & acrylonitrile was packed wet into the solid-state rotor via tabletop centrifugation. Solid-state quantitative multi-cross-polarization (CP) experiments were acquired with a Bruker Avance IIIHD 600MHz (14.1T) NMR spectrometer equipped with a 3.2 mm triple-resonance (HXY) DNP probe tuned in ^{1}H-^{13}C double mode (Johnson & Schmidt-Rohr, 2014). Quantitative multi-CP experiments with 11 ms total CP duration and 10,240 scans were calibrated on an external standard (*N*-acetyl-valine) for a total experimental time of 19.5 hrs. each.

6.3.6. Statistical Analysis

Statistical analyses were preformed using the software JMP 16 and included a one-way analysis of variance test and a Tukey-Kramer HSD test.

6.4. Results

6.4.1. Durability

Curaplex and Ansell Life Star brand EMT gloves (n = 5) withstood the most sandpaper touches before rupturing, with averages of 246 and 245 touches, respectively

(Figure 6.1.). Restore Touch and Vglove branded examination gloves were the least durable, withstanding averages of 24.2 and 7.2 touches, respectively (Figure 6.1.). A one-way ANOVA test ($\alpha = 0.5$) revealed that at least one glove brand had a significantly different average number of touches to failure ($P = 0.009$). The subsequent Tukey-Kramer HSD test showed that the means from the following brands were significantly different from each other: Curaplex and Vglove ($P = 0.0289$), Ansell Life Star and Vglove ($P = 0.0453$), and Curaplex and Restore Touch ($P = 0.0487$).

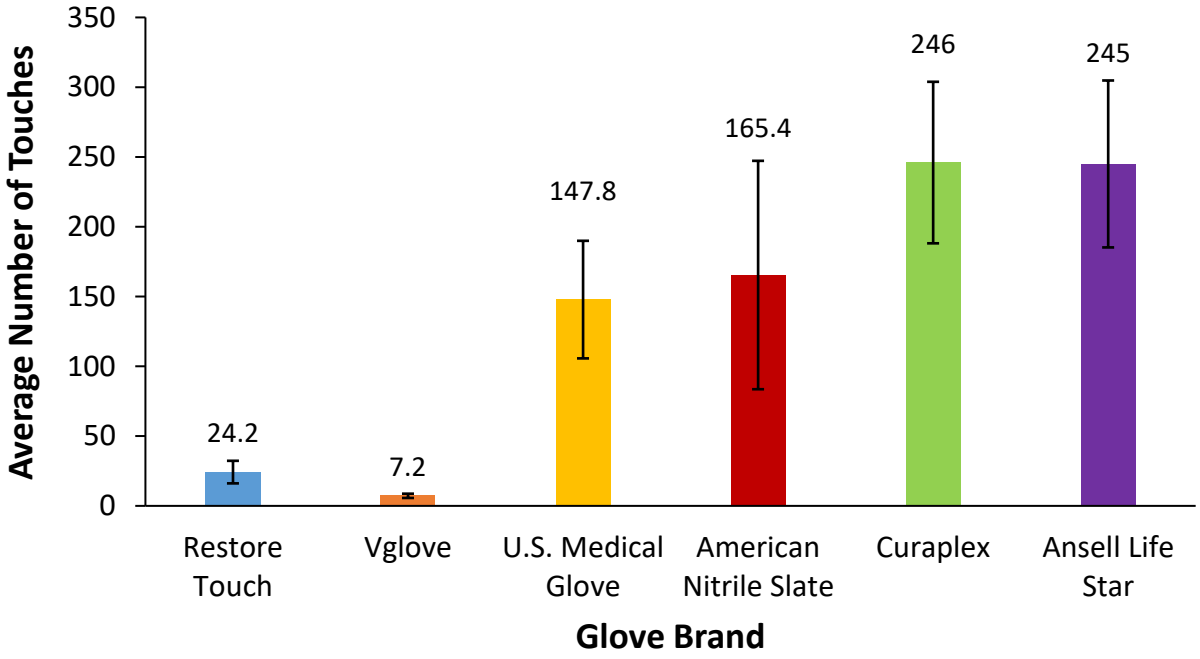


Figure 6.1. Number of sandpaper touches to glove failure for Restore Touch, Vglove, U.S. Medical Glove, American Nitrile Slate, Curaplex and Ansell Life Star brands, with n = 5 $\pm$ standard error (n = 4 $\pm$ standard error for Ansell Life Star due to limited number of samples.)

The thinnest gloves on average were Restore Touch brand, with a mean of 0.078 mm (Figure 6.2.). The single thinnest glove overall was also a Restore Touch brand

glove, with a fingertip thickness of 0.06 mm. This value is barely above the minimum ASTM thickness requirement for nitrile examination gloves, 0.05 mm. All other glove brands measured far exceeded the ASTM minimum (Figure 6.2.). It has previously been reported that Restore Touch and Vglove cuff thickness fell below 0.05 mm (average values of 0.043 mm and 0.048 mm, respectively.) (Thomas et al., 2011).

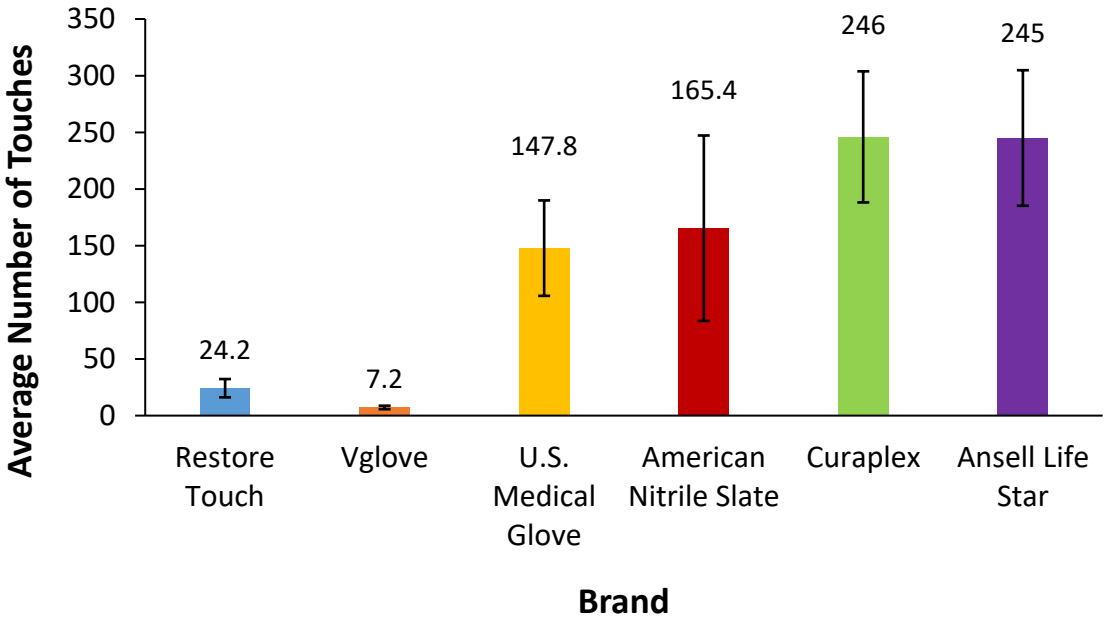


Figure 6.2. Average fingertip thickness for Restore Touch, Vglove, U.S. Medical Glove, American Nitrile Slate, Curaplex and Ansell Life Star brands, with n = 5 ± standard error (n = 4 ± standard error for Ansell Life Star.) The horizontal line represents the ASTM minimum acceptable glove thickness for nitrile examination gloves, 0.06 mm.

6.4.2. Mechanical Properties

Evaluation of tensile strength demonstrated that Restore Touch and Vglove had the poorest mechanical properties, with Restore Touch samples breaking between 586% and 697% elongation and Vglove samples between 458% and 632% elongation (Figure 6.3.). In contrast, U.S. Medical Glove samples generally broke above 800% elongation,

with the exception of one extreme outlier that broke at only 435% elongation and so was removed from the data set (Figure 6.3.). The American Nitrile Slate brand glove dumbbells broke between 413% and 518% elongation. The two EMT Curaplex and Ansell Life Star glove samples, broke between 450% and 837% and between 574% and 931% elongation, respectively.

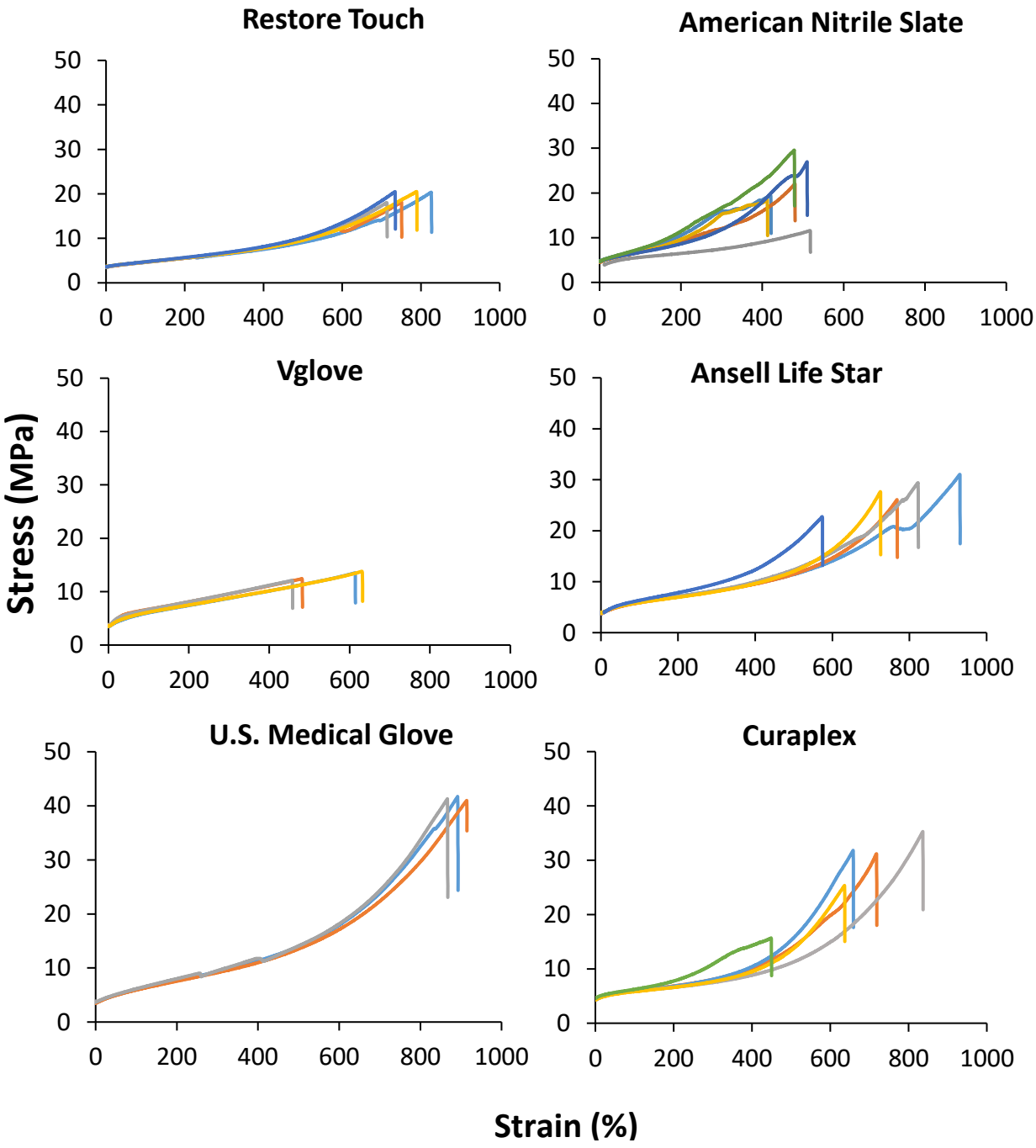


Figure 6.3. Tensile stress versus tensile strain for gloves described on their boxes as nitrile examination gloves for 4 glove brands (Restore Touch, American Nitrile Slate, Vglove, and U.S. Medical Glove), and nitrile EMT gloves for 2 glove brands (Ansell Life Star and Curaplex). Samples were cut using dumbbell Die C. The point at which the plots end is where the testing dumbbell broke in two.

6.4.3. FTIR Analysis

Characteristic FTIR peaks of NBR were labeled according to those specified in previous studies of the spectrum of NBR (Alhareb et al., 2017; Liang et al., 2019; Samantarai et al., 2019). The peak at 2235 cm^{-1} corresponds to the characteristic nitrile (C≡N) group of NBR (Figure 6.4.). Other notable peaks include the =C-H butadiene group at 967 cm^{-1} and -C-H group at 1438 cm^{-1} (Figure 6.4.). These peaks act as a baseline for comparison for the unknown glove samples. Although all of these characteristic peaks are present in the glove samples, the samples also contain peaks that are not present in the FTIR spectrum of pure nitrile, indicating the presence of materials other than NBR (Figure 6.5.).

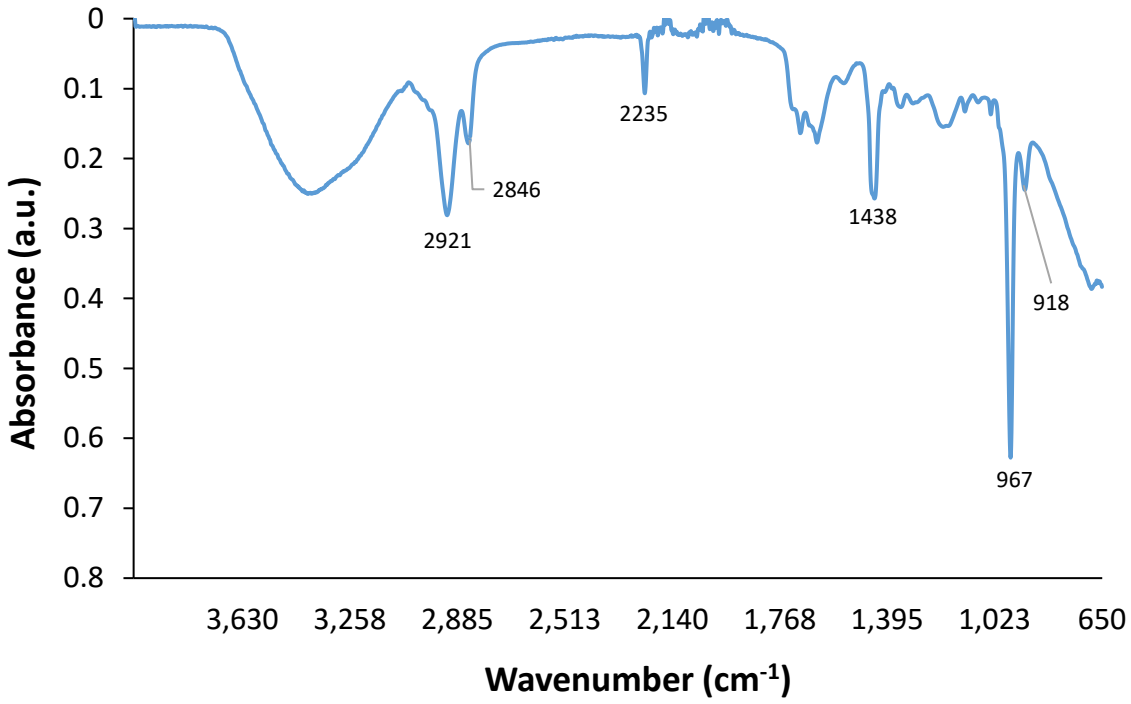


Figure 6.4. FTIR absorbance data for pure nitrile with characteristic peaks labeled.

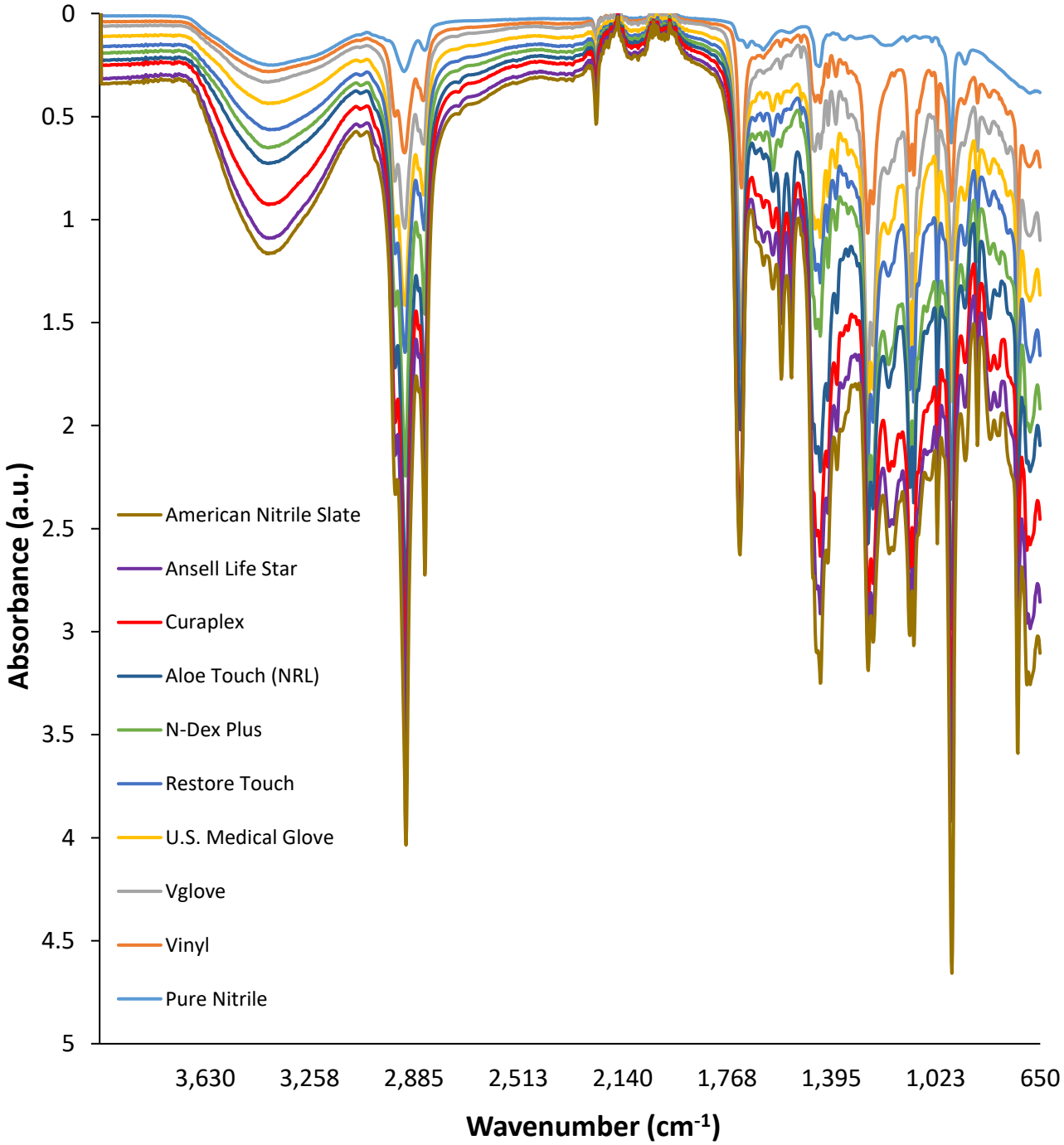


Figure 6.5. FTIR absorbance data for Vglove, U.S. Medical Glove, Restore Touch, N-Dex Plus, Curaplex, Ansell Life Star, and American Nitrile Slate brand gloves compared to the positive and negative controls: pure nitrile and vinyl (PVC), respectively. A natural latex glove (*Hevea* latex) was also added as a reference.

The FTIR absorbance spectra demonstrate a large amount of overlap, even among glove brands made from different polymers. Natural *Hevea* latex was included as a reference in order to demonstrate that even a glove made from a natural polymer has very similar FTIR peaks to the synthetic nitrile gloves. The industrial-grade N-Dex Plus glove was included as an additional reference because it is a non-medical nitrile glove. The authors suspect that this large amount of similarity may be due to chemical additives that are universal to the glove manufacturing process. Therefore, the FTIR analyses of the gloves was found to be inconclusive because they did not definitively identify gloves as pure nitrile, as they all claim to be.

6.4.4. NMR Analysis

Pure nitrile rubber (dried from an aqueous dispersion of butadiene and acrylonitrile) has clear ^{13}C chemical shift signature peaks centered around 33.7 ppm and 132.5 ppm, with the latter corresponding to alkenes found in the 1,2 (-C=) polymer and the 1,4 (-C=) polymer (Figure 6.6.). In addition, any C≡N alkyne site would fall within this chemical shift range. This NMR spectral signature of nitrile is found in N-Dex Plus, Restore Touch, U.S. Medical, and all three American Nitrile gloves (Figure 6.6.).

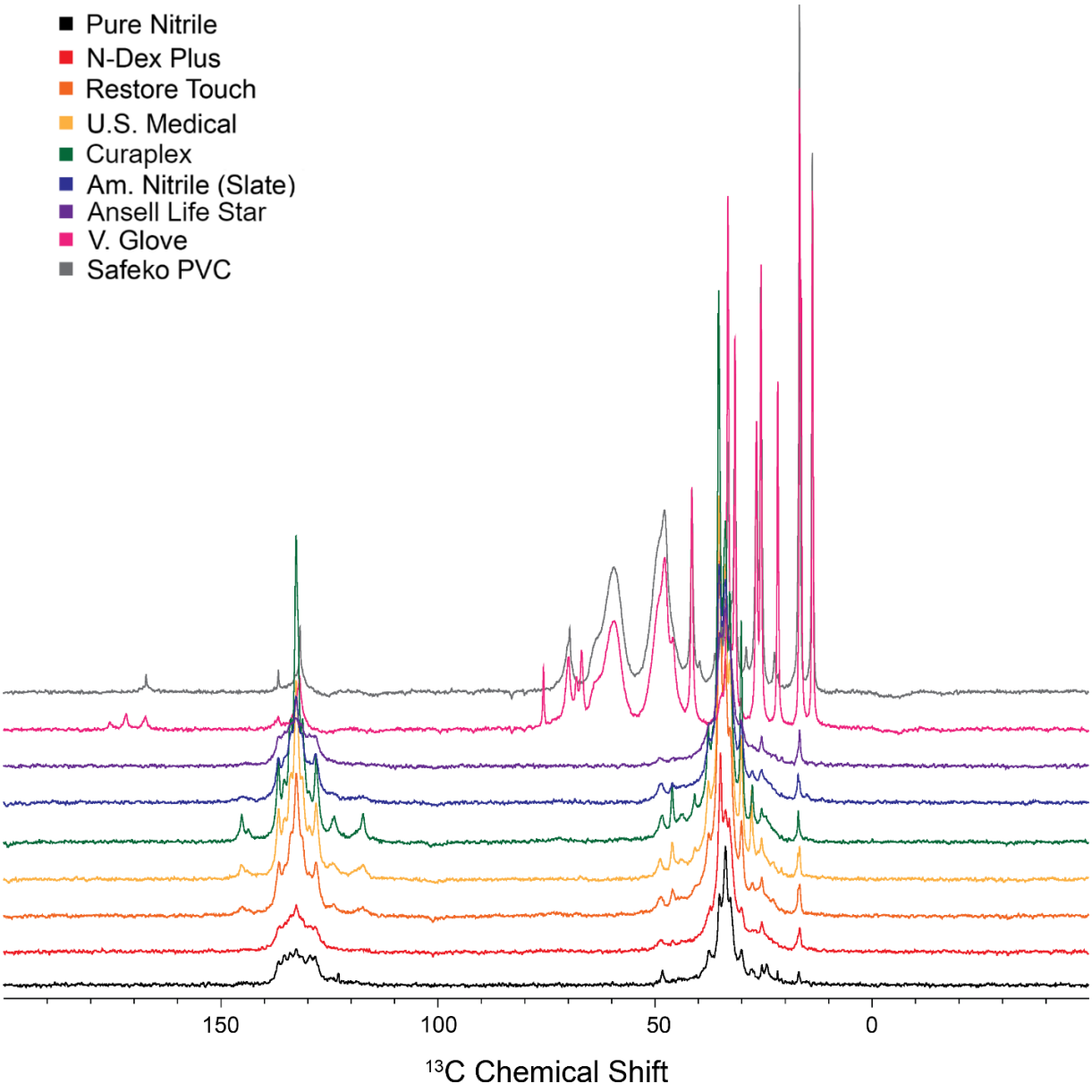


Figure 6.6. NMR spectra for Vglove, U.S. Medical Glove, Restore Touch, N-Dex Plus, Curaplex, Ansell Life Star, and American Nitrile Slate brand gloves. Safeko brand PVC gloves and pure nitrile were also included as positive and negative controls, respectively.

The Safeko PVC glove was analyzed to provide the ^{13}C chemical shift signature of polyvinyl chloride (PVC) and shows a clearly different ^{13}C NMR spectrum than that of

nitrile, despite overlaps with nitrile rubber due to peaks centered at 131.7 ppm and 33.1 ppm (Willoughby, 1988). In PVC, signature peaks of 47.8 ppm and 59.4 ppm can be associated with the CHCl units and the CH_2 units of the CHCl-CH_2Cl sites of PVC, respectively (Nakayama et al., 1994). Vglove possessed an NMR spectral signature that was nearly identical to Safeko PVC and is therefore consistent with a primarily or entirely PVC composition (Figure 6.7.).

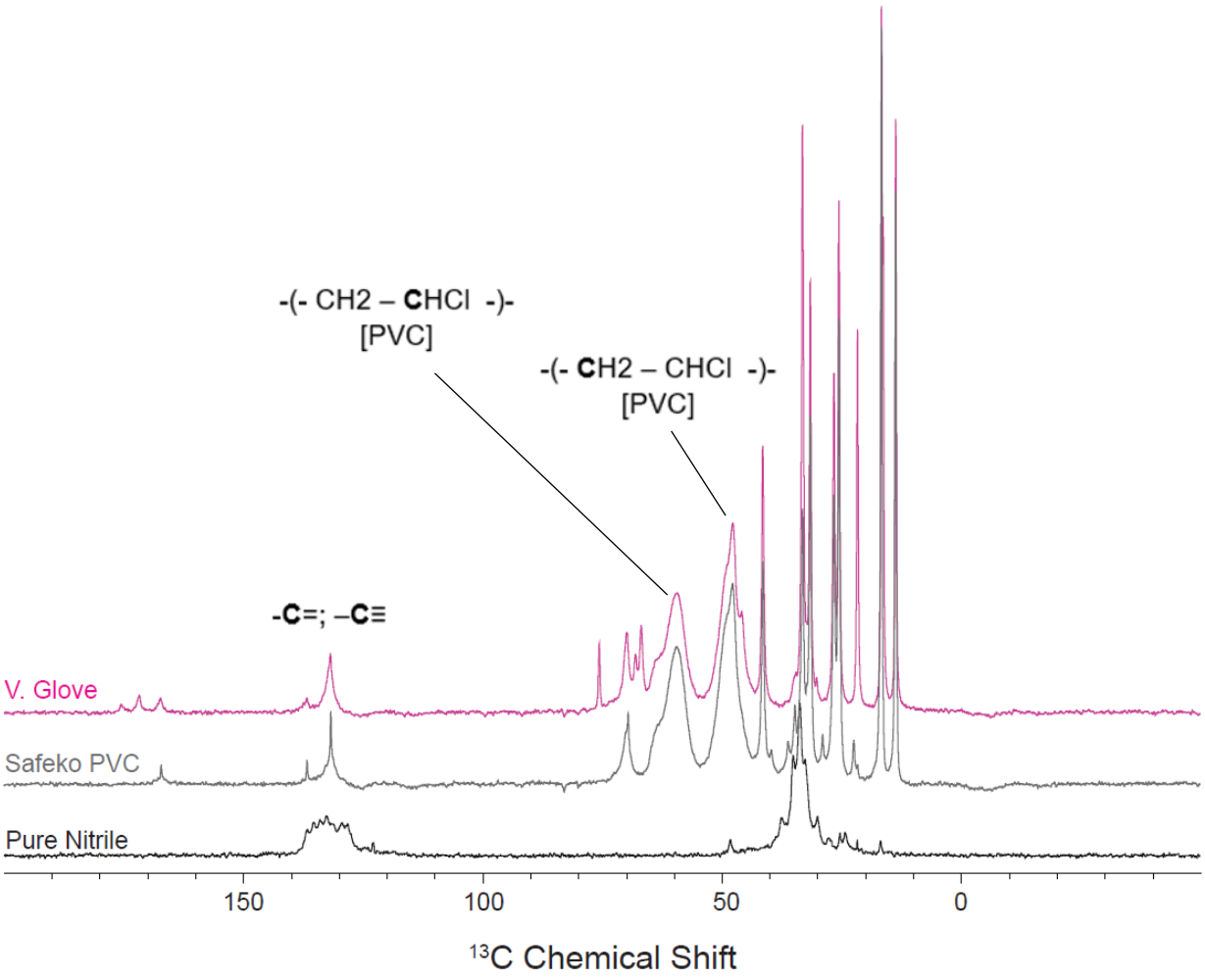


Figure 6.7. NMR spectrum for Vglove compared to Safeko PVC and pure nitrile spectra. Signature peaks of PVC and their corresponding chemical structures are labeled.

6.4.5. ASTM Standards

ASTM International standard D6319 specifies minimum values for tensile strength, thickness, and elongation to break for nitrile medical examination gloves (ASTM International 2019e). Upon comparing the lowest data values collected to the minimum values set by ASTM, Vglove brand glove failed to meet the requirements for both tensile strength (12.11 MPa, compared to a 14 MPa minimum) and elongation to

break (458%, compared to 500% minimum) (Table 6.1.). The lowest percent elongation value for American Nitrile Slate gloves also did not reach the 500% elongation minimum, failing at only 413% elongation (Table 6.1.). Two out of the six samples tested exceeded the minimum elongation requirement, while the others did not (Figure 6.3.).

Restore Touch brand gloves, although exceeding the minimum tensile strength and elongation requirements, were barely thicker than the minimum thickness requirements at only 0.06 mm compared to the ASTM minimum of 0.05 mm (Table 6.1.). U.S. Medical Glove brand exceeded all minimum requirements set by ASTM International (Table 6.1.).

Table 6.1. Lowest mechanical property values collected for each nitrile glove brand and minimum values specified by ASTM standard D6319. All tensile strength values collected for the Vglove brand fell below the required minimum of 14 MPa.

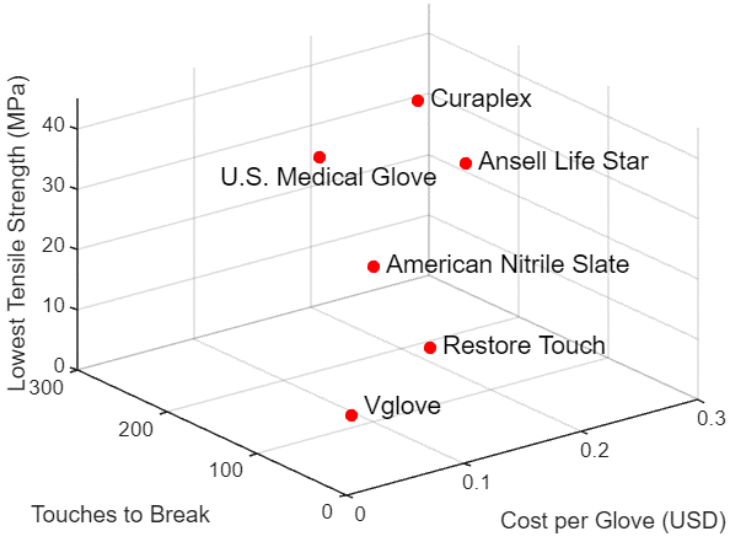
Glove Brand	**Tensile Strength (MPa)**	**Thickness (mm)**	**Elongation to Break (%)**
Restore Touch	18.03	0.06	714
Vglove	12.11	0.09	458
U.S. Medical Glove	40.99	0.12	867
American Nitrile Slate	18.46	0.10	413
Curaplex*	35.28	0.18	837
Ansell Life Star*	22.75	0.17	574
ASTM Minimum Value	**14**	**0.05**	**500**

*****Curaplex and Ansell Life Star gloves were included in this table because ASTM International does not have a standard specifically for EMT gloves.

A comparison of cost and mechanical properties reveals that only the poor performance Vglove was markedly lower cost than the other gloves (Figure 6.8.). The cost used are retail prices. We have not attempted to take into account price savings

accrued through bulk purchasing. The Restore Touch glove was slightly cheaper than the U.S. Medical Glove and American Nitrile Slate gloves but was much thinner (Figure 6.2.) suggesting a higher profit margin – at the expense of quality. These two American manufacturers are making much higher performance nitrile gloves than Restore Touch. Their only potential downside is that tactile sensation through these gloves may be less than through the Restore Touch.

a)



b)

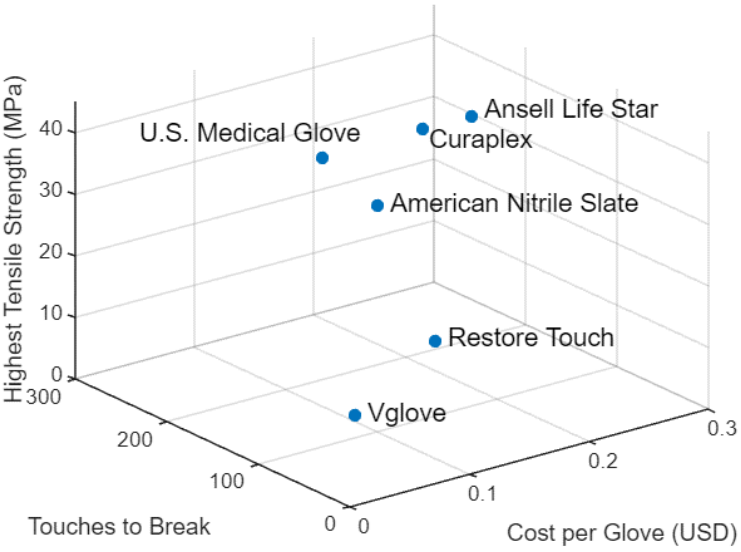


Figure 6.8. Comparison of cost per glove, durability (number of touches to break), and a) lowest recorded tensile strength values (MPa) and b) highest recorded tensile strength values (MPa) for Restore Touch, Vglove, U.S. Medical Glove, American Nitrile Slate, Curaplex, and Ansell Life Star.

6.5. Discussion

The variability in composition and mechanical performance of nitrile medical examination gloves is cause for serious concern. The NMR spectrum of Vglove provides strong evidence that their "nitrile examination glove" is primarily or entirely made from PVC. This mislabeling also explains its inability to meet the minimum requirements set by ASTM International for nitrile examination gloves. In a previous study in which the durability and mechanical properties of several varieties of medical gloves were compared, PVC gloves were found to be less durable, less stretchy, and less strong than high-quality nitrile gloves (Thomas et al., 2011). A company blog post written in 2020 by Elara Brands brought attention to the issue of fraudulent PPE during the COVID-19 pandemic. It stated that the name "Vglove" is a trademark of a legitimate company and that scammers were using the name to sell apparently counterfeit nitrile gloves that were actually made of PVC (*Elara Brands, Avoid Fake Gloves to Safeguard Your Business*). These claims are in accordance with the findings of the current study.

Although the NMR spectrum of Restore Touch brand gloves was consistent with that of pure nitrile, the gloves still preformed relatively poorly on the durability test. This poor performance was likely due to the thinness of the gloves, at an average of 0.078 mm and a minimum value of 0.06 mm, which is just above the ASTM minimum requirement of 0.05 mm for nitrile exam gloves (ASTM International 2019e). In a previous study, samples of this same glove type and brand were found to have an average cuff thickness less than 0.05, which shows that Restore Touch has also failed to meet ASTM

requirements (Thomas et al., 2011). Even a tear the size of a pinhole can allow pathogenic viruses and bacteria, some of which are deadly, to transfer through the medical glove. It is well known that nitrile glove films tear very easily once a break is initiated (Thomas et al., 2011), so even a small rupture can quickly lead to a complete glove failure. This study also demonstrated a positive correlation between glove thickness and durability, which further supports this explanation (Thomas et al., 2011).

The thicker nitrile gloves used by EMTs face the unique challenge of protecting the wearer from exposure to dangerous drugs like fentanyl, a synthetic opioid 50 to 100 times more potent than morphine (*Fentanyl DrugFacts*), which is readily absorbed by the human body due to its small size (336.5 Da) (*Fentanyl: Incapacitating Agent*), in addition to blood-borne pathogens. According to the National Center for Health Statistics at the Center for Disease Control and Prevention, fentanyl and other synthetic opioids are now the most common drugs involved in overdose deaths in the United States, with 70,601 deaths in 2021 (*Drug Overdose Death Rates*). The two brands of EMT gloves evaluated in this study demonstrated both to be suitably strong and durable, although both were quite thick, which reduces tactile sensation by the wearer's hands.

This study has demonstrated that considerable variation in glove quality and performance exists among different brands of nitrile gloves. Although we have not tested all supposed nitrile glove currently in the marketplace, we have proved that Vglove brand nitrile gloves are not made of pure nitrile. This suggests that there may be other nitrile glove brands that are actually made of PVC (Figure 6.7.). The relatively low durability of Restore Touch brand gloves, which are made of nitrile (Figure 6.6.), is because these

gloves are very thin, barely meeting minimum thickness requirements set by ASTM International. In contrast, the high-performance nitrile examination gloves made by US Medical Glove were almost as strong and durable as the thick EMT gloves. It is likely that other properties of the gloves such as heat resistance, oxygen aging resistance, solvent resistance also vary. However, these only become relevant in a glove that remains intact during normal use, so were not tested here.

Future studies will include analyses of the mechanical performance and NMR spectra of a wider variety of nitrile medical glove brands to gain a more complete understanding of the quality of gloves on the market. An analysis of the mechanical performance of gloves exposed to common solvents will also be conducted.

6.6. Conclusions

The marketing of substandard gloves can have serious consequences for healthcare workers who rely on personal protective equipment such as medical gloves to protect themselves and their patients from healthcare-associated infections (HAIs). Therefore, gloves that fail to meet even the minimum requirements set by ASTM International and the FDA should not be used for medical purposes. The authors urge those who regularly use nitrile examination gloves to emphasize glove quality over other considerations to adequately protect themselves and their patients.

6.7. Acknowledgements

The authors thank EnergyEne, Inc. for permission to use the GAD device in this study. We also thank U.S. Medical Glove and American Nitrile for generously donating their gloves to be used this study. This work was supported by the USDA National Institute of Food and Agriculture, OHO01524, accession 7003189.

Chapter 7. Medical Glove Durability is Differentially Affected by Solvent Exposure Impacting User Safety

This chapter is based on the following manuscript:

Herkins, A., & Cornish, K. (2024). Medical Glove Durability is Differentially Affected by Solvent Exposure Impacting User Safety. Patient Safety in Surgery. Under Review. (Peer Reviewed)

This chapter demonstrates the use of the Glove Assessment Device described in Chapter 4 to test the durability of medical gloves in phosphate buffered saline, 70% ethanol, and deionized water. These solvents simulate substances that healthcare workers frequently encounter that may alter the barrier effectiveness of their medical gloves. The gloves that performed best in Chapter 5 were selected for this study. As the first author, I was primarily responsible for experimental design, data collection and analysis, and drafting the manuscript.

7.1. Abstract

Medical professionals are constantly exposed to bodily fluids and sanitizing agents during routine medical procedures. Unbeknownst to many healthcare workers, however, the barrier integrity of medical gloves can be altered when exposed to these substances, potentially resulting in the spread of life-threatening bacteria and viruses. This study quantifies the relative durability of a sample of commercially available medical gloves exposed to 70% ethanol, phosphate buffered saline, deionized water, and

air in order to simulate the environments in which medical gloves are commonly worn. The glove assessment device automatically detects pinhole-sized perforations in medical gloves, eliminating the need to visually inspect each glove. Interestingly, most gloves performed better when exposed to solvents than in air, which is likely due to slippage in the interface between the wet glove and the sandpaper. Sensicare Micro, a polyisoprene surgical glove, had the most consistent durability in all three solvents tested. A two-way ANOVA revealed that both glove brand ($P = 0.0001$), solvent ($P = 0.0001$), and their interaction ($P = 0.0040$, $\alpha = 0.05$) significantly affected average glove durability. These results make it clear that additional testing and labeling information would help healthcare workers select gloves for use in specific environments to ensure best barrier protection against disease or toxins.

7.2. Introduction

The critical role of medical gloves in disease prevention was highlighted during the COVID-19 pandemic when the demand for these essential protective items doubled in the United States, leading to widespread shortages (*Medical Device Shortages List*). Previous studies have shown that glove durability varies greatly depending on glove material, type, thickness, usage time, and manufacturer, and that substandard gloves put the health of safety of healthcare workers and patients at risk (Bardorf et al., 2016; Herkins & Cornish, 2023; *Medical Device Shortages List*; Michel & Cornish, 2016; Tlili et al., 2018). However, not all durability studies account for the fact that medical professionals frequently encounter fluids such as saliva, blood, and disinfectants that may

alter the physical properties of their medical gloves, potentially reducing their effectiveness as protective barriers.

The mechanical properties of medical gloves have been demonstrated to change depending on solvent exposure. A study on the durability of natural and synthetic medical gloves that had been exposed to phosphate buffered saline (PBS), ethanol, and air concluded that relative glove performance depended upon the solvent (if any) in which the glove had been submerged (Michel & Cornish, 2015). The order of failure for solvent-exposed gloves does not necessarily match the failure order of dry gloves (Herkins & Cornish, 2023; Michel & Cornish, 2015). Another study demonstrated that the application of alcohol-based hand rubs to nitrile and latex examination gloves resulted in decreased tensile strength and increased ultimate elongation, particularly of the nitrile samples (Gao et al., 2016).

The objective of this study was to utilize an automated glove assessment device (Venturini et al., 2022) to determine the relative durability of natural and synthetic medical gloves exposed to common medical solvents in order to simulate glove use in realistic environments.

7.3. Materials and Methods

7.3.1. Gloves

The gloves selected for this study were chosen because they had been previously demonstrated to have superior durability in dry conditions (Herkins & Cornish, 2023). Synthetic gloves included U.S. Medical Glove (nitrile examination gloves), Montgomery,

IL, USA, Sensicare Neoprene (polychloroprene surgical gloves; Medline), Northfield, IL, USA, and Sensicare Micro (polyisoprene surgical gloves; Medline), Northfield, IL, USA. The natural latex gloves included Triumph Micro (latex surgical gloves; Medline), Northfield, IL, USA and Aloe Touch (latex examination gloves; Medline), Northfield, IL, USA. Glove sizes were selected to fit securely on the prosthetic hand of the GAD, namely, sizes medium and large or numerical sizes 6-8. Five trials were conducted for each sample/solvent combination with the exception of Sensicare Micro polyisoprene surgical gloves tested in PBS, which had four trials only due to one defective glove. Thicknesses were an average of three measurements taken at the middle finger of the glove.

7.3.2. Glove Assessment Device (GAD)

The Glove Assessment Device (GAD) that was used to determine relative glove durability eliminates the need to manually inspect gloves for holes, or perform a water leak test, because it relies on a vacuum within the base of a prosthetic hand, which creates a seal when a glove is donned (Venturini et al., 2022). The two middle fingers of the hand are porous, allowing airflow into the base of the hand only when a puncture occurs in the glove. A pressure sensor causes the GAD to automatically cease operation when a pressure spike occurs due to a perforation in the glove. To induce a perforation, the GAD uses a strip of 120-grit waterproof sandpaper clamped onto a mobile drum that touches the fingertips of the prosthetic hand repeatedly at a set force. The sandpaper was replaced for each new glove tested. The liquid spray functionality of the GAD was used to simulate medical environments more realistically. All settings on the GAD were set to

default (Venturini et al., 2022) apart from the sprayer, which was set to spray the glove fingers once between each touch of the sandpaper drum.

7.3.3. Solvents

The selected solvents were deionized water, phosphate buffered saline (PBS solution, Fisher Scientific, Pittsburgh, PA, USA), and 70% ethanol solution (Fisher Scientific, Pittsburgh, PA, USA). PBS closely mimics properties of human bodily fluids, including ion concentration, osmolarity, and pH. Ethanol is commonly used as a cleaning agent and disinfectant in medical facilities. DI water was used as a reference liquid and was also used to cleanse the tubing of the GAD when changing solvents.

7.3.4. Statistical Analysis

The software JMP 16 was used for all statistical analyses in this study. These analyses include a two-way analysis of variance and Tukey-Kramer HSD tests. The two independent variables tested were glove type and solvent, and the independent variable was the average number of sandpaper touches until glove failure.

7.4. Results

Glove durability differed drastically depending on the type of solvent to which the glove was exposed, with the exception of Sensicare Micro brand polyisoprene surgical gloves which had a consistent performance in all three solvents (Figure 7.1.). Gloves exposed to solvents of any kind generally were more durable than gloves tested in air (Figure 7.1.). Most surgical gloves performed better than exam gloves in all three solvents; however, the Aloe Touch brand natural latex exam gloves had very similar

durability to the Triumph Micro latex surgical gloves (Figure 7.1.). This result indicates that material plays an important role in solvent-exposed glove durability, regardless of glove usage type (surgical or exam). The U.S. Medical Glove brand nitrile exam glove was also the only glove to perform better in air than in one of the solvents, in this case PBS (Figure 7.1.).

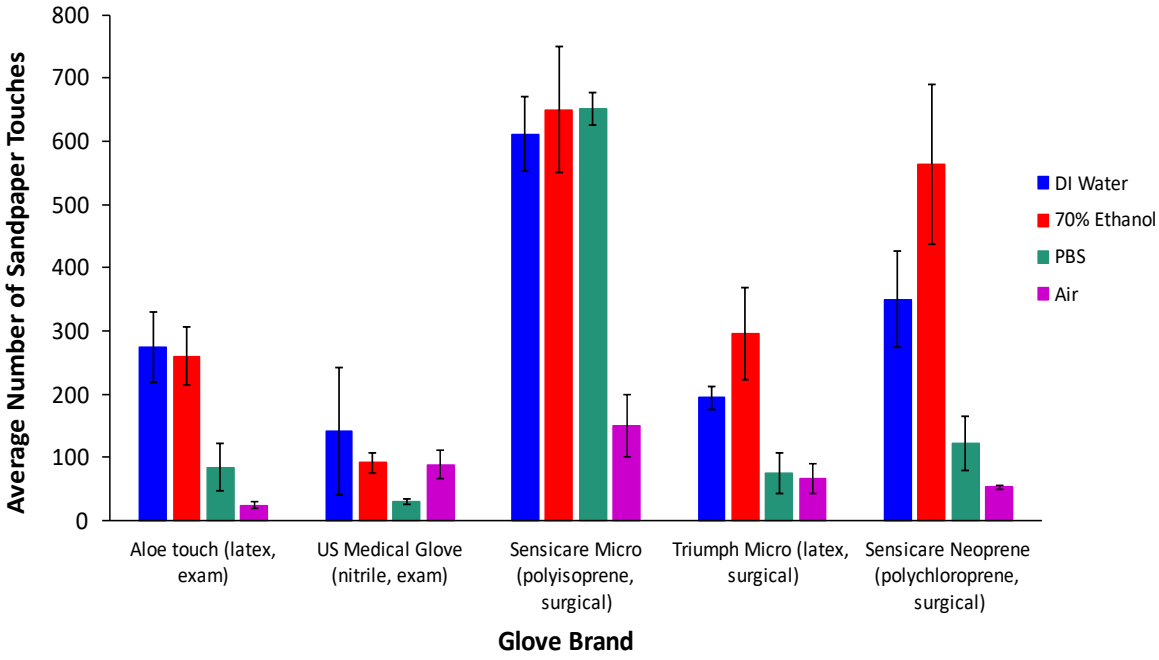


Figure 7.1. Average number of sandpaper touches until glove failure in DI water, 70% ethanol, PBS, and air ± standard error. Labeled values represent the mean of 5 samples except for Sensicare Micro polyisoprene surgical gloves tested in PBS, which had four trials only due to a defective glove.

The two-way ANOVA revealed that at least one factor was significant (P = 0.0001). The subsequent effects test showed that glove type (P = 0.0001), solvent (P = 0.0001), and their interaction (P = 0.0040) all significantly affected durability (average number of sandpaper touches to failure). The Sensicare Micro polyisoprene surgical

glove lasted significantly longer than the other gloves under testing (Tukey's HSD test, Table 7.3.). Gloves tested in PBS and air had significantly different average number of touches than the other two test treatments (Table 7.2.). The connecting letters report for the cross effect of glove type and solvent revealed that no singular glove/solvent combination resulted in a significantly different least square mean from all other combinations (Table 7.3.).

Table 7.1. Connecting letters report of Tukey's HSD test of glove type. Levels not connected by the same letter are significantly different.

Glove Type				Least Squares Mean
Sensicare Micro (polyisoprene, surgical)	A			637.20
Sensicare Neoprene (polychloroprene, surgical)		B		345.40
Aloe Touch (latex, exam)		B	C	206.13
Triumph Micro (latex, surgical)		B	C	188.16
U.S. Medical Glove (nitrile, exam)			C	87.47

Table 7.2. Connecting letters report of Tukey's HSD test of solvent type. Levels not connected by the same letter are significantly different.

Solvent			Least Squares Mean
70% Ethanol	A		372.08
DI Water	A		314.16
PBS		B	192.73
Air		B	81.55

Table 7.3. Connecting letters report of Tukey's HSD test of the cross effect of glove type and solvent type. Levels not connected by the same letter are significantly different.

Glove Type, Solvent						Least Squares Mean
Sensicare Micro (polyisoprene, surgical), PBS	A	B				651.0
Sensicare Micro (polyisoprene, surgical), 70% Ethanol	A					649.8
Sensicare Micro (polyisoprene, surgical), DI Water	A	B	C			610.8
Sensicare Neoprene (polychloroprene, surgical), 70% Ethanol	A	B	C	D		563.6
Sensicare Neoprene (polychloroprene, surgical), DI Water	A	B	C	D	E	350.2
Triumph Micro (latex, surgical), 70% Ethanol		B	C	D	E	295.8
Aloe Touch (latex, exam), DI Water			C	D	E	274.4
Aloe Touch (latex, exam), 70% Ethanol				D	E	259.6
Triumph Micro (latex, surgical), DI Water					E	194.0
Sensicare Micro (polyisoprene, surgical), Air					E	175.8
U.S. Medical Glove (nitrile, exam), DI Water					E	141.4
Sensicare Neoprene (polychloroprene, surgical), PBS					E	122.4
U.S. Medical Glove (nitrile, exam), 70% Ethanol					E	91.6
U.S. Medical Glove (nitrile, exam), Air					E	88.8
Aloe Touch (latex, exam), PBS					E	84.4
Triumph Micro (latex, surgical), PBS					E	74.7
Triumph Micro (latex, surgical), Air					E	65.7
Sensicare Neoprene (polychloroprene, surgical), Air					E	53.3
U.S. Medical Glove (nitrile, exam), PBS					E	29.4
Aloe Touch (latex, exam), Air					E	24.2

Surgical gloves are usually thicker than examination gloves and have higher mechanical performance requirements than exam gloves (ASTM D3578-19 and D3577-19) and so are expected to have greater durability (ASTM International 2019a, 2019b). However, although Sensicare Neoprene brand polychloroprene surgical gloves were the thickest gloves out of those tested, they were the second least durable in air and they were less durable than the Sensicare Micro brand polyisoprene surgical gloves in all solvents (Figure 7.2.).

Sensicare Micro (polyisoprene, surgical) and Sensicare Neoprene (polychloroprene, surgical) brand gloves were of similar thickness, but had drastically different durability under most testing conditions (Figure 7.2.). Similarly, U.S. Medical Glove brand nitrile exam gloves and Aloe Touch brand latex exam gloves were the same thickness but did not have similar durability. Thus, although thickness does play a role in glove durability, thickness alone is not indicative of how long a glove will last before rupturing, especially when gloves are exposed to solvents (Figure 7.2.).

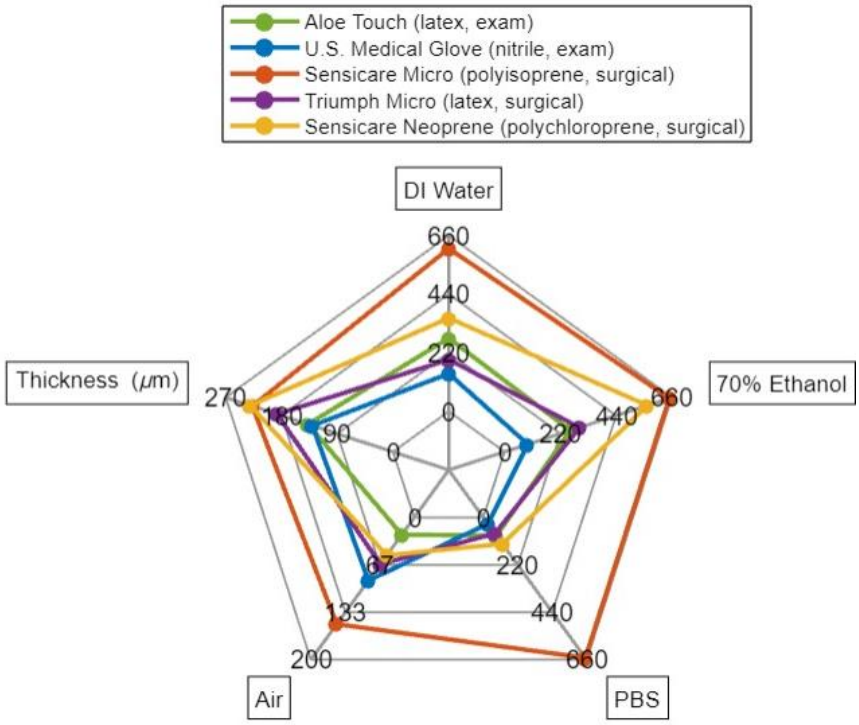


Figure 7.2. Radar plot of the average number of sandpaper touches to failure in DI water, 70% ethanol, PBS, and air. Glove thickness (μm) is also included for reference. Numeric labels represent the scale of the radar plot. Note: the axis for air in not the same scale as those for DI water, ethanol, and PBS.

7.5. Discussion

Average glove durability was generally lower in air than in any of the solvents tested. The likeliest explanation for this phenomenon is the presence of slippage within the sandpaper/glove interface when liquids are introduced. The solvents likely acted as lubricants, lessening the interaction of the abrasive sandpaper with the glove film.

ASTM International provides specific standards which all examination gloves (D3578-19) and surgical gloves (D3577-19) must meet, regardless of whether they are made of natural (Type I) or synthetic (Type II) polymers (ASTM International 2019a,

2019b). Because the sampled gloves have previously been confirmed to meet these standards, substandard glove quality can be ruled out as a cause of durability differences (Herkins & Cornish, 2023).

The large variation in durability observed between gloves of similar thickness indicates that the composition of the glove, and not solely its thickness, is responsible for its performance, as has been previously concluded (Herkins & Cornish, 2023; Walsh et al., 2004). One explanation for the gloves failing more readily in PBS than in other solvents is that PBS is hydrophobic, which may allow greater penetration into the gloves, and acting as a plasticizer. This may also account for why the U.S. Medical Glove brand nitrile exam glove performed more poorly in PBS than in air. Also, natural latex gloves contain non rubber constituents, including protein and lipids. The PBS may extract entrained proteins and perturb the cured glove matrix making it less durable (Siler et al., 1997; Wood & Cornish, 2000).

The durability of the two natural latex gloves tested (Aloe Touch exam and Triumph Micro surgical) were more similar in the three solvents than in air because the liquid-polymer interaction is consistent in gloves made of the same material.

A significant factor in solvent permeation through medical gloves is movement, which could not be simulated by the GAD. Latex gloves have been previously demonstrated to have similar ethanol permeation rates regardless of movement (Phalen et al., 2014). In contrast, the permeation of ethanol through nitrile gloves was significantly higher when the gloves were flexed during solvent exposure (Phalen et al., 2014). Since the gloves tested on the GAD were placed on a stationary prosthetic hand, the true glove

barrier effectiveness is expected to decrease when the gloves are worn on the hands of healthcare providers.

The implications of these findings are extremely important for healthcare professionals who regularly wear medical gloves, especially during surgical procedures. A glove that remains intact in air could have an entirely different barrier effectiveness when exposed to bodily fluids or sanitizing agents. Micro perforations as small as 27 nm can allow for the transfer of the smallest human pathogenic viruses resulting in the spread of healthcare-associated infections (HAIs) (Cornish & Lytle, 1999). Therefore, it appears that additional testing and labeling information may be needed so that healthcare professionals can select gloves that provide the best barrier protection in specific environments against disease or toxins for themselves and their patients.

7.6. Conclusions

Durability of gloves that were most durable in air is heavily influenced by solvent exposure, glove material, glove thickness, and glove usage type. During medical procedures where gloves are exposed to bodily fluids and disinfecting agents, reduced glove barrier efficiency can lead to the spread of potentially life-threatening healthcare associated infections. Future studies should include a much larger sample of commercially available medical gloves to provide healthcare professionals with a more complete representation of relative glove performance in solvents, drugs, and air.

7.7. Acknowledgements

The authors thank EnergyEne, Inc. for permission to use the GAD device in this study. We also thank U.S. Medical Glove for generously donating their gloves to be used this study. This work was supported by the USDA National Institute of Food and Agriculture, OHO01524, accession 7003189.

Chapter 8. Accelerant Optimization for Circumallergenic Guayule Latex Endotracheal Tube Cuff

The physical properties and hypoallergenic nature of guayule latex make it an ideal biomaterial not only for medical gloves, but also for endotracheal tube balloon cuffs. These cuffs must be soft, strong, and durable so that they can make a perfect seal between the cuff and the tracheal wall and prevent bacterial drainage into the lungs of intubated patients and subsequent ventilator associated pneumonia. In this chapter, a hypoallergenic xanthate-based accelerant system is optimized to create a high-strength, low-modulus guayule latex endotracheal tube cuff. As the first author, I was primarily responsible for experimental design, data collection and analysis, and drafting the manuscript. Sarah Davis, a research scientist at EnergyEne Inc., provided training on the Diplomat automated dipper, assisted with sample dipping, and provided training on the tensiometer.

8.1. Abstract

Endotracheal tube (ETT) balloons are important for maintaining the health and safety of intubated patients. The balloon, which surrounds part of the tracheal tube, is intended to hold the tube in place in the trachea. Ideally, the inflated balloon also creates a seal between the ETT and the tracheal wall, preventing bacteria-laden saliva drainage into the lungs which can cause pneumonia. ETT balloons are commonly made of hard

plastics such as polyvinyl chloride (PVC). If a PVC balloon is overinflated it can damage the cells of the tracheal lining. Unless the balloon forms a perfect fit with the trachea when fully inflated, pleats remain through which saliva can drain into the lungs of the patient, which is usually the case. As a solution to these issues, ETT cuffs made from soft, hypoallergenic guayule latex placed outside the PVC balloon and sealed to the tracheal tube were previously developed but have not been commercialized. Although these outer cuffs do not cross-react with Type I latex allergy, they were made using conventional vulcanization chemicals which can cause adverse contact reactions. New outer cuffs have been made with guayule latex using a xanthate-based accelerant system designed to avoid contact reactions. A combination of 2.0 parts per hundred rubber (phr) diisopropyl xanthogen polysulphide (DIXP) and 0.6 phr zinc diisononyl dithiocarbamate (ZDNC) resulted in the highest tensile strengths in both thin and thick ETT cuffs (39.50 MPa and 42.35 MPa, respectively). The lowest modulus values occurred at 2.0 phr DIXP and 0.8 ZDNC for thinner samples and 2.2 phr DIXP and 1.0 phr ZDNC for thicker samples (1.92 MPa and 1.83MPa, respectively.) A leak test was conducted for the guayule ETT cuffs, and the resulting two-way ANOVA revealed no significant effect of accelerant concentration on leakage rate ($P = 0.5783$). Thus, all cuffs prevented leakage consistently. Finally, varying the size of the simulated trachea for the PVC cuffs revealed that larger tracheas had lower average leak rates due to the increased room for the cuff to expand, reducing the number of longitudinal folds.

8.2. Introduction

Contact reactions to chemicals, including Type IV allergic dermatitis, are characterized by skin reactions such as rash and papules, often with a delayed onset of symptoms. Following initial contact with the antigen, the immune system generates antigen-specific, sensitized T lymphocytes (Pak et al., 2012). Once sensitized, a person may experience symptoms if exposed to even small concentrations of antigen that would otherwise have no effect on non-sensitized individuals (Pak et al., 2012). The two types of contact reactions are allergic contact dermatitis, in which the body responds to an antigen with an allergic reaction, and irritant contact dermatitis, in which the body responds to an irritating substance by creating a rash.

Natural rubber accelerators and antioxidants, like thiurams, mercapto benzathiazoles (MBT), and thiocarbonates, which are used to reduce the cure time and temperature during the vulcanization process (Pak et al., 2012), are common agents of occupational contact reactions and allergic dermatitis (Meyer et al., 2000).

In addition to Type IV allergies, Type I allergies, or immediate hypersensitivity reactions, are a concern with natural latex tapped from the Para rubber tree (*Hevea brasiliensis*). If not properly leached, *Hevea* rubber contains sensitizing levels of the antigenic proteins that induce Type I latex allergies (Cornish, 2012). Latex from the guayule shrub (*Parthenium argentatum*), however, naturally contains no sensitizing latex proteins, making it safe for those with existing Type I latex allergies (Cornish, 2012; Siler et al., 1996). It is also very low in immunogenic protein, making it extremely unlikely that a new guayule-specific allergy will arise in users (Cornish, 2012).

Guayule latex is an ideal material for medical devices not only because it is hypoallergenic, but because of its superior softness, stretchiness, strength, and durability (Cornish et al., 2008; Herkins & Cornish, 2023). In devices such as endotracheal tube (ETT) cuffs, this combination of properties is ideal for the efficacy of the device and patient safety. When a patient is intubated, the balloon attached around the ETT is inflated to hold the tube in a patient's throat. A perfect seal between the ETT and the tracheal wall is needed to prevent mucus and saliva from seeping into the patient's lungs and causing ventilator associated pneumonia (VAP), a life-threatening condition. Leakage occurs when a PVC ETT balloon is sufficiently inflated to hold the tracheal tube in place but has remaining pleats because the patient's trachea is smaller in diameter than the fully inflated diameter of the balloon (Figure 8.1.).

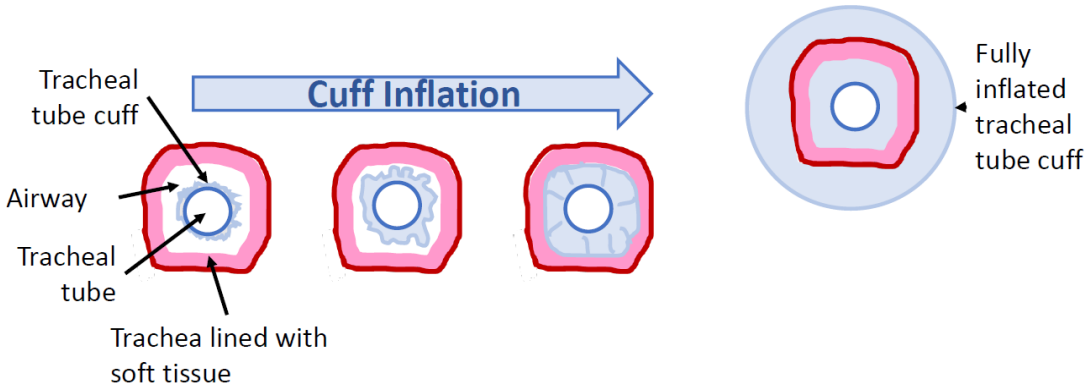


Figure 8.1. PVC endotracheal tube balloons are plastic and so do not form a perfect seal with the tracheal wall when inflated because the balloon is larger than the tracheal diameter.

It is estimated that between 8% to 28% of mechanically ventilated patients develop VAP (Hamilton & Grap, 2012) due to leakage through balloon pleats. Treatment costs of VAP are estimated to be between $10,000 and $40,000 per patient in the United

States (Luckraz et al., 2018) and the mortality rate is 30-70% (Chouhdari et al., 2018). Though it may seem that VAP may be preventable by increasing the air pressure within the cuff, overinflation can cause severe damage to the tracheal tissue (Moon et al., 2022).

A benchtop study found that prototype guayule latex endotracheal tube cuffs placed outside the PVC pleated balloon prevented leaks (Zanella et al., 2008). However, these cuffs were made with conventional accelerators which can cause contact irritation and dermatitis. In this study, we have optimized a xanthate-based accelerator package, developed to not cause contact reactions in humans (Chakraborty & Couchman, 2006) for a guayule latex ETT cuff in order to minimize the cuff's modulus of elasticity, maximize tensile strength, and prevent ETT leakage.

8.3. Methods

8.3.1. Formulation and Dipping

Preliminary experiments were performed to determine the ratios of diisopropyl xanthogen polysulphide (DIXP) and zinc diisononyl dithiocarbamate (ZDNC) that best combined low Young's Modulus with high tensile strength and elongation because ETT cuffs must be soft to not injure the tracheal wall, but strong and stretchy enough to prevent leakage without breaking when the interior PVC balloon is inflated. Several combinations were tested (Table 8.1.).

Table 8.1. Concentrations of DIXP and ZDNC and curing system used in dipped sample cuffs.

DIXP (phr)	ZDNC (phr)	Dwell Time (s)	Average Thickness (mm)	
2.0, 2.2	0.6, 0.8, 1	5, 15	0.13, 0.16	
GNRL (phr)	NH4OH	Antioxidant	ZnO	Sulfur
100.0	0.7	2.3	0.5	3.2

Samples were dipped to a depth of 12 cm via a Diplomat automated dipper (DipTech Systems Inc., Kent, OH, USA) using 13 mm diameter glass rods as formers. Dwell times of 5 and 15 seconds were used to vary the thickness of the samples, with the longer dwell time resulting in thicker samples (Table 8.1.). The complete curing procedure is as follows:

1. Place 13 mm ID glass rods (formers) into an oven set at 70°C.
2. Attach glass rods to the Diplomat and dip 8 cm into the coagulant. Return formers to the oven for 25 min.
3. Attach formers to the Diplomat and dip 12 cm into GNRL compound for either 5 or 15 seconds. Return formers to oven for 30 min.
4. Leach the formers in a 70°C water bath for 4 min.
5. Hand-dip formers in polyurethane coating. Increase oven temperature to 104°C.

6. Place formers into 104°C oven for 40 min.

7. Remove samples from formers. Tumble dry on low heat for 1 hr.

8.3.2. Tensile Tests

Tensile tests were conducted according to ASTM D412 using Die D (ASTM International 2021). Four dumbbell samples were cut from each cured guayule latex cuff for a total of 48 samples. Dumbbells were tested 14 days after they were made using an Instron 3366 (250 N maximum load cell) with Bluehill v. 2.17 software package (Instron, Norwood, MA, USA). Crosshead speed was set to 500 mm/min, and all tests were conducted at room temperature (26°C).

8.3.3. Trachea Size Variation Tests

Three cylindrical acrylic tubes of internal diameters (IDs) 16 mm, 20 mm, and 22 mm were used to simulate three sizes of human tracheas. A Curaplex brand polyvinyl chloride endotracheal tube with balloon attached (Bound Tree Medical, Dublin, OH, USA) was used for this study. The simulated trachea was held in place on a ring stand, and the ETT was inserted. Tube cuffs were inflated to 30 cm H_2O, as this is the highest pressure that will not damage the tracheal wall tissue (Moon et al., 2022). An AG Cuffill® barometer (Hospitech Respiration, Kfar Saba, Israel) was used to measure the cuff pressure. Two drops of food coloring were added to a 150 mL beaker of water to increase visibility during testing. A liquid collection beaker was placed beneath the apparatus, and 15 mL of colored water was added to the top of the simulated trachea (Figure 8.2.). The volume of fluid in the collection beaker was measured via a 15 mL

graduated cylinder after 15 min or after all the fluid had leaked, whichever occurred first. Leakage rate was recorded as volume per minute. This procedure was repeated three times for each size trachea.

Figure 8.2. Benchtop setup of the apparatus during a PVC cuff leak test.

8.3.4. Guayule Cuff Leak Test

The procedure for the guayule cuff leak test was the same as that for the unmodified ETT, except that a guayule cuff was placed on top of the existing PVC balloon. Approximately 0.5 mL of sterile surgical gel (Surgilube, Altana Inc., Melville, NY, USA) was used to lubricate the cuff and fill the gap between them. The uniform

interface between the two cuffs due to the lubricant ensured that no pressure hot spots were present in the outer cuff. The guayule latex cuff was secured using dental floss to simulate surgical sutures. The inner tube cuff was inflated until the outer cuff formed an initial seal with the side of the tube (Figure 8.3.). Three replicate leak tests were performed for each variety of guayule latex tube cuff.

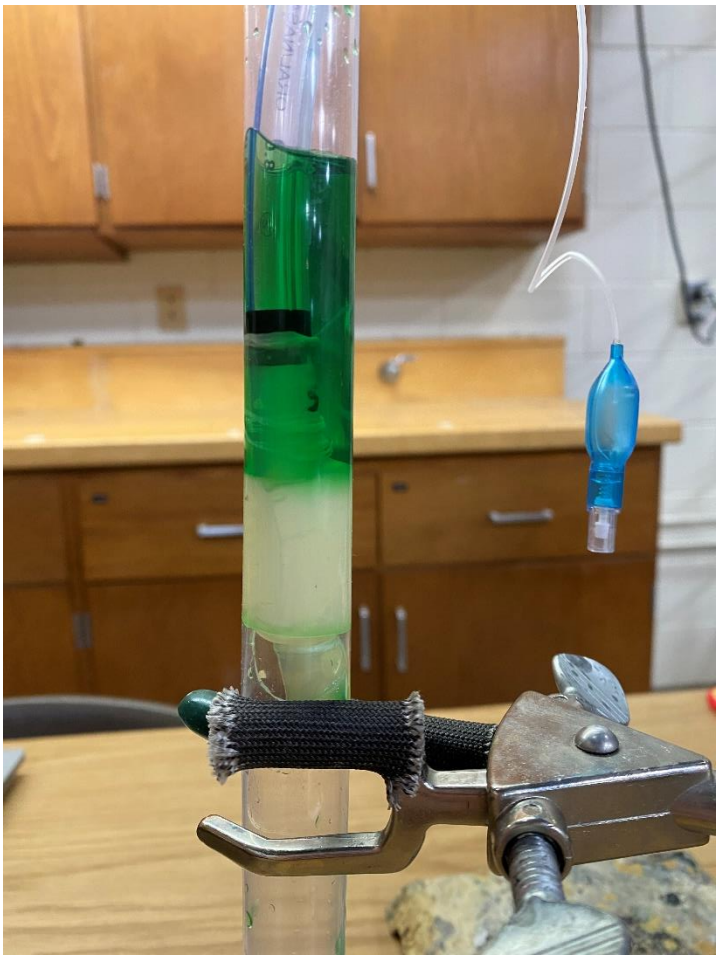


Figure 8.3. Guayule latex tube cuff applied over inflated PVC cuff during leak test.

8.3.5. Statistical Analysis

The statistical software JMP 16 was used for all statistical analysis, including one-way and two-way ANOVA tests and a Tukey's HSD test.

8.4. Results

8.4.1. Tensile Test

The highest tensile strength for both dwell times resulted from the lowest concentrations of both ZDNC (0.6 phr) and DIXP (2.0 phr) (Table 8.2.). The same samples also had the highest ultimate elongation values. The lowest average Modulus value for the 5-second dwell time samples was 1.92 MPa, occurring in samples with 2.0 phr DIXP and 0.8 phr ZDNC (Table 8.2.). The lowest average Modulus value for the 15-second dwell time samples was 1.83, which occurred in samples with 2.2 phr DIXP and 1.0 phr ZDNC (Table 8.2.).

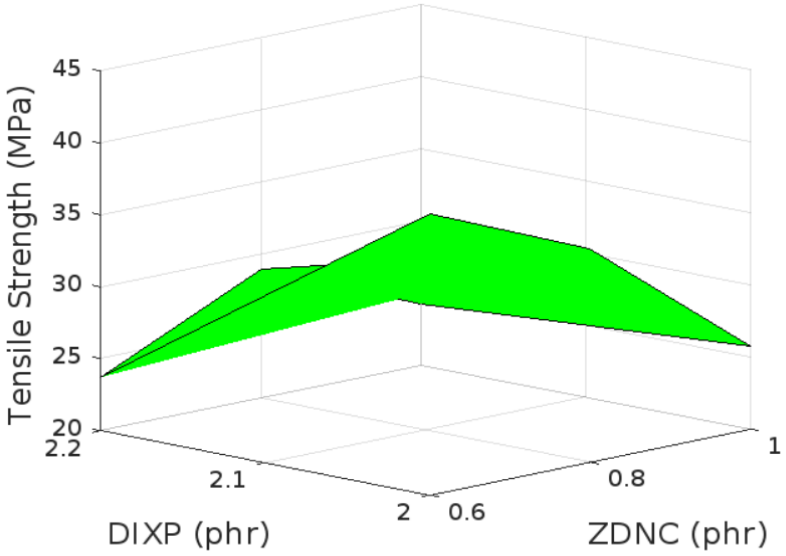
Table 8.2. Average values of modulus at 500% elongation, ultimate elongation, tensile strength, and thickness for all accelerant combinations and dwell times (n = 4).

Dwell Time (sec)	ZDNC (phr)	DIXP (phr)	Modulus at 500% Elongation (MPa)	Ultimate Elongation (%)	Tensile Strength (MPa)	Thickness (mm)
5	0.6	2.0	2.04	2012.34	39.50	0.13
	0.8	2.0	1.92	2001.52	34.79	0.14
	1.0	2.0	2.05	1859.03	25.76	0.12
	0.6	2.2	2.30	1791.73	23.72	0.11
	0.8	2.2	1.99	1942.24	28.94	0.14
	1.0	2.2	2.08	1779.94	24.26	0.14
15	0.6	2.0	1.85	2192.99	42.35	0.17
	0.8	2.0	1.88	1973.29	30.63	0.16

1.0	2.0	2.07	1906.99	23.38	0.15
0.6	2.2	1.92	2129.83	39.39	0.16
0.8	2.2	1.92	1968.28	28.81	0.16
1.0	2.2	1.83	1839.18	24.86	0.18

The overall effect of accelerator concentration on tensile strength varied depending on dwell time (Figure 8.4.). For both dwell times, however, the highest tensile strengths occurred in the samples made with concentrations of 2.0 phr DIXP and 0.6 phr ZDNC (Figure 8.4.).

a)



b)

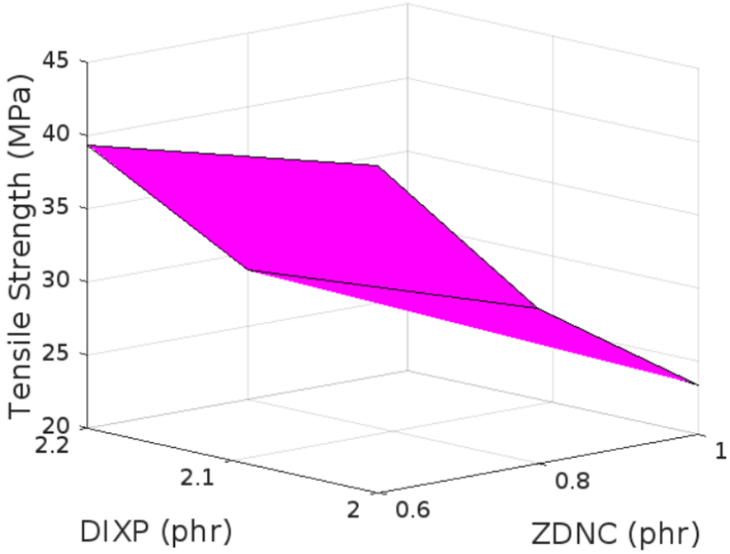


Figure 8.4. 3D surface plots of DIXP (phr), ZDNC (phr), and average tensile strength (MPa) for ETT cuffs with a a) 5 second dwell time and b) 15 second dwell time.

8.4.2. Trachea Size Variation Test

The larger the diameter of the simulated trachea, the lower the average leak rate (Figure 8.5.). The standard error was also the largest for the 16 mm ID tube tests,

indicating that the results were less consistent than those of the 20 mm and 22 mm tube tests (Figure 8.5.).

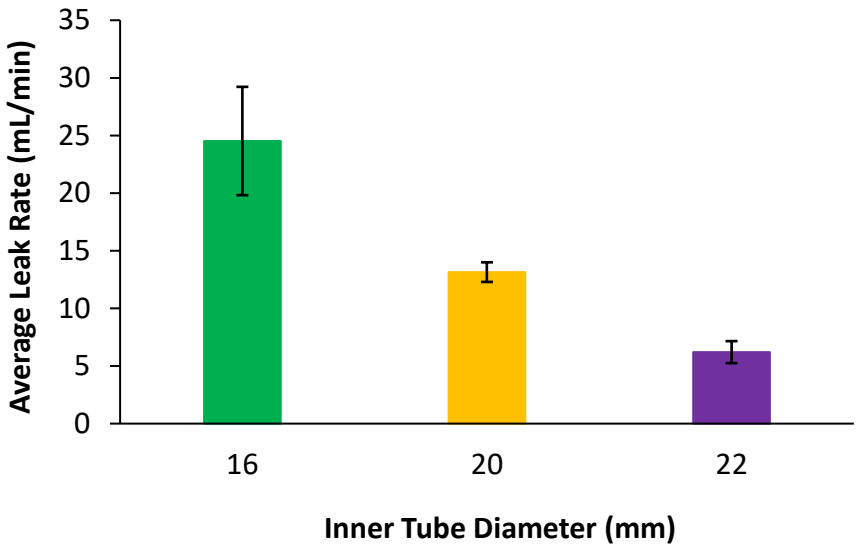


Figure 8.5. Inner diameter of the simulated trachea (mm) vs. average leak rate (mL/min). Error bars represent ± standard error.

A one-way ANOVA resulted in a P-value of 0.0253, indicating that at least one of the values was significantly different. A Tukey's HSD test for inner tube diameter revealed that the average leakage rate for the 16 mm ID tube and the 22 mm ID tube were significantly different (Table 8.3.). The leakage rate for the 20 mm ID tube was not found to be significantly different from either of the other two samples (Table 8.3.).

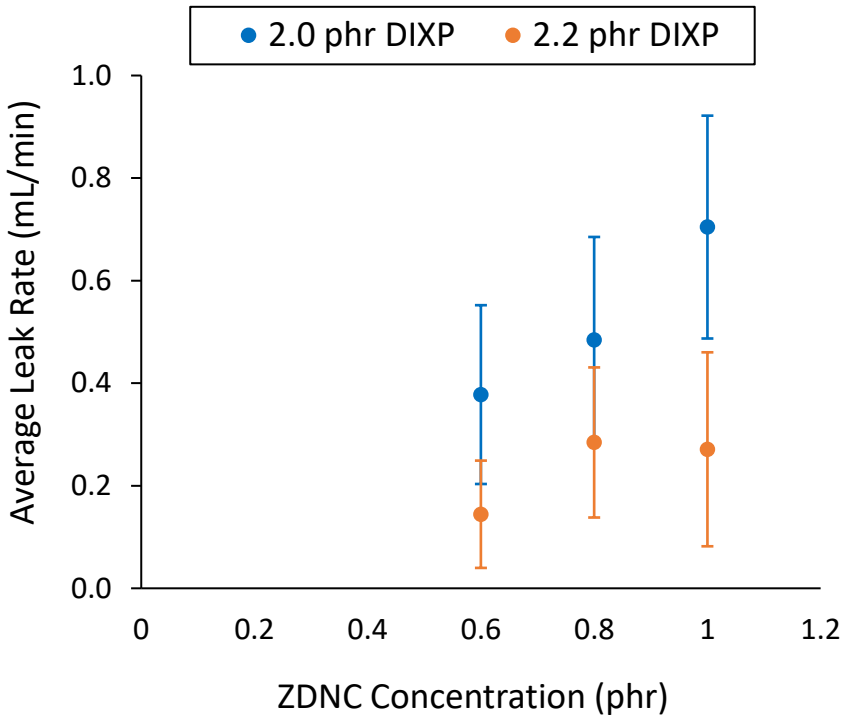
Table 8.3. Connecting letters report of Tukey's HSD test for inner tube diameter (mm). Levels not connected by the same letter are significantly different.

Tube Diameter (mm)		Least Square Mean
16	A	24.52
20	A B	13.14
22	B	6.20

8.4.3. Benchtop Leak Tests

Of the 5-second dwell time samples, the lowest average leakage rate occurred in the samples with accelerant concentrations of 2.2 phr DIXP and 0.6 phr ZDNC (Figure 8.6.). As for the 15-second dwell time samples, accelerant concentrations of 2.0 phr DIXP and 0.8 phr ZDNC resulted in the lowest average leak rate (Figure 8.6.). The leak rate was 0 mL/min for 2 of the 5-second dwell time samples 8 and of the 15-second dwell time samples. A two-way ANOVA revealed that ZDNC and DIXP concentration did not significantly affect average leak rate ($P = 0.5783$).

a)



b)

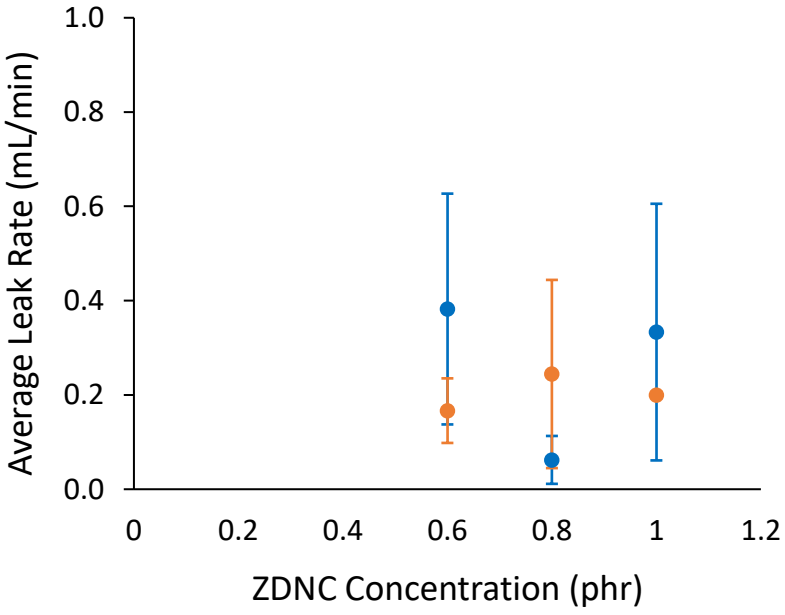


Figure 8.6. Average leak rate (mL/min) vs. concentration of ZDNC and DIXP (phr) for a) 5-second dwell time samples and b) 15-second dwell time samples. Error bars represent ± standard error.

8.5. Discussion

For both the thin and thick cuffs, accelerant concentrations of 2.0 phr DIXP and 0.6 phr ZDNC resulted in samples with the highest tensile strength, which agrees with the results of preliminary film tests. All samples had a Young's Modulus below 2.3 MPa, indicating that they are all sufficiently soft to avoid strain crystallization (Fig. 5.6) upon sufficient inflation (2.6 mL to 3.3 mL for 20 cm H_2O) to reach the tracheal wall, which would harden the cuff (Sengupta et al., 2004). The two-way ANOVA found no significant impact of DIXP and ZDNC concentrations on leak rate ($P = 0.5783$). It is therefore inferred that leak rate is relatively consistent regardless of accelerant concentration. Thus, the samples created with 2.0 phr DIXP and 0.6 phr ZDNC are ideal because of their high tensile strength and elongation, low modulus, and excellent leak prevention.

The larger leak rate associated with a smaller trachea size is likely due to the higher folding into pleats. In a larger trachea, there is more space for the balloon to fully inflate. Longitudinal folds, even in fully inflated cuffs, increase leakage (Young et al., 1997). Selecting an appropriately sized ETT cuff is vital for the device to limit bacteria-laden salvia and mucus drainage into the lungs and prevent pressure-induced damage to the trachea. Smaller patients, particularly women, are more susceptible to iatrogenic postintubation tracheal ruptures caused by incorrect ETT sizing (Sudhoff et al., 2015).

Leakage into the trachea can be result from both defective and intact ETT balloons. The most common causes of airway leaks in non-defective cuffs include underinflation, cephalad migration of endotracheal tube, tracheal misplacement of

nasogastric tubes, wide discrepancy between endotracheal tube and tracheal diameters, and high peak airway pressure (El-Orbany & Salem, 2013). It has also been found that duration of prior intubation and absence of sedation are independently associated with increased risk for cuff underinflation for ICU patients (Nseir et al., 2009).

8.6. Conclusion

Guayule latex endotracheal tube (ETT) cuffs produced using a xanthate-based accelerant system provide solutions to many of the challenges of synthetic cuffs. The cuffs discussed in this study are circumallergenic because they induce neither a Type I nor a Type IV latex allergy. They are also strong, soft, stretchy, and excellent at preventing leaks - all properties that are ideal for an ETT cuff. The accelerant combination that produced the strongest and most leak proof outer balloon cuff was 2.0 parts per hundred rubber (phr) diisopropyl xanthogen polysulphide (DIXP) and 0.6 phr zinc diisononyl dithiocarbamate (ZDNC). If adopted by the healthcare industry, these cuffs have the potential to save hospitals and patients thousands of dollars each year and prevent deaths caused by ventilator-associated pneumonia.

8.7. Acknowledgements

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Chapter 9. Conclusion

The objectives of this research were to develop and test circumallergenic guayule latex biomedical products and to determine the physical properties of new and existing products via a Glove Assessment Device (GAD) and other methods. An invention disclosure for the GAD was submitted to the Ohio State University in the spring of 2021. ASTM International is also moving forward with a medical glove durability standard that incorporates the GAD. This is an important step toward accountability for the medical glove manufacturers that are risking the safety of healthcare workers through the production of inadequate products. The substandard gloves identified in this research, such as the falsely labeled Vglove, should be immediately discontinued by healthcare professionals for safety reasons.

Future research will include streamlining the design of the GAD, including the incorporation of a permanent rough surface, interchangeable hand sizes, and improved user interface. Once a second prototype is finalized, it will be sold to glove manufacturers and incorporated as a standard quality check in the glove manufacturing process. Using the data reported in this research, the prototype guayule latex exam and surgical gloves can be marketed to healthcare facilities as physically superior to even *Hevea* latex gloves with the additional benefit of being allergen-free. Similarly, the accelerant-optimized

guayule latex endotracheal tube cuff can be marketed as a safer alternative to synthetic cuffs due to its superior leak prevention and hypoallergenic accelerant system.

Overall, the development of high-quality rubber medical devices is key in preventing deadly healthcare-associated infections such as ventilator associated pneumonia and COVID-19, among many others. This research provides strong evidence for the safety and effectiveness of hypoallergenic guayule-latex medical devices, brings attention to underperforming rubber medical products, and delineates a device designed to be incorporated as a universal part of the glove manufacturing process.

Bibliography

Abraham, E. K., & Ramesh, P. (2002). Natural Rubber Latex Products: Concerns in Health Care. *Journal of Macromolecular Science, Part C*, *42*(2), 185-234. https://doi.org/10.1081/MC-120004763

Actor, J. K. (2023). Chapter 8 - Immune hypersensitivities. In J. K. Actor (Ed.), *Introductory Immunology (Third Edition)* (pp. 123-131). Academic Press. https://doi.org/https://doi.org/10.1016/B978-0-443-15307-5.00011-1

Ahrends, A., Hollingsworth, P. M., Ziegler, A. D., Fox, J. M., Chen, H. F., Su, Y. F., & Xu, J. C. (2015). Current trends of rubber plantation expansion may threaten biodiversity and livelihoods. *Global Environmental Change-Human and Policy Dimensions*, *34*, 48-58. https://doi.org/10.1016/j.gloenvcha.2015.06.002

Albin, M. S., Bunegin, L., Duke, E. S., Ritter, R. R., & Page, C. P. (1992). Anatomy of a defective barrier: sequential glove leak detection in a surgical and dental environment. *Crit Care Med*, *20*(2), 170-184.

Alhareb, A., Akil, H., & Ahmad, Z. (2017). Poly(methyl methacrylate) denture base composites enhancement by various combinations of nitrile butadiene rubber/treated ceramic fillers. *Journal of Thermoplastic Composite Materials*, *30*(8), 1069-1090. https://doi.org/10.1177/0892705715616856

Andrade, K. L., Ramlow, H., Floriano, J. F., Acosta, E. D., Faita, F. L., & Machado, R. A. F. (2022). Latex and natural rubber: recent advances for biomedical applications. *Polímeros*, *32*.

ASTM International (2016). D6699-16 Standard Practice for Sampling Liquids Using Bailers.

ASTM International (2018). D6499-18 Standard Test Method for Immunological Measurement of Antigenic Protein in Hevea Natural Rubber (HNR) and its Products.

ASTM International (2019a). D3577-19 Standard Specification for Rubber Surgical Gloves.

ASTM International (2019b). D3578-19 Standard Specification for Rubber Examination Gloves.

ASTM International (2019c). D5151-19 Standard Test Method for Detection of Holes in Medical Gloves.

ASTM International (2019d). D5250-19 Standard Specification for Poly(vinyl chloride) Gloves for Medical Application.

ASTM International (2019e). D6319-19 Standard Specification for Nitrile Examination Gloves for Medical Application.

ASTM International (2019f). D6977-19 Standard Specification for Polychloroprene Examination Gloves for Medical Application.

ASTM International (2020a). D624-00(2020) Standard Test Method for Tear Strength of Conventional Vulcanized Rubber and Thermoplastic Elastomers.

ASTM International (2020b). D5712-15(2020) Standard Test Method for Analysis of Aqueous Extractable Protein in Latex, Natural Rubber, and Elastomeric Products Using the Modified Lowry Method.

ASTM International (2021). D412-16(2021) Standard Test Methods for Vulcanized Rubber and Thermoplastic Elastomers- Tension.

Bardorf, M. H., Jager, B., Boeckmans, E., Kramer, A., & Assadian, O. (2016). Influence of material properties on gloves' bacterial barrier efficacy in the presence of microperforation. *Am J Infect Control*, *44*(12), 1645-1649. https://doi.org/10.1016/j.ajic.2016.03.070

Bown, C. P. (2022). How COVID-19 Medical Supply Shortages Led to Extraordinary Trade and Industrial Policy. *Asian Economic Policy Review*, *17*(1), 114-135. https://doi.org/https://doi.org/10.1111/aepr.12359

Chaiprapat, S., & Sdoodee, S. (2007). Effects of wastewater recycling from natural rubber smoked sheet production on economic crops in southern Thailand. *Resources Conservation and Recycling*, *51*(3), 577-590. https://doi.org/10.1016/j.resconrec.2006.11.003

Chakraborty, K. B., & Couchman, R. (2006). Technological and physico-chemical behavior of safer accelerators in synthetic polyisoprene latex. *17*, 1-12.

Chouhdari, A., Shokouhi, S., Bashar, F. R., Vahedian Azimi, A., Shojaei, S. P., Fathi, M., Goharani, R., Sahraei, Z., & Hajiesmaeili, M. (2018). Is a Low Incidence Rate of Ventilation Associated Pneumonia Associated with Lower Mortality? a Descriptive Longitudinal Study in Iran. *Tanaffos*, *17*(2), 110-116.

Continental Tire. *Natural Rubber from Dandelions: Taraxagum*. Retrieved March 21, 2024 from https://www.continental-tires.com/about/sustainability/activities-and-initiatives/material-sourcing/taraxagum/

Cornish, K. (2012). Assessment of the Risk of Type I Latex Allergy Sensitization or Reaction During Use of Products Made From Latex Derived from Guayule and Other Alternate Rubber Producing Species. *Rubber Science*, *25*(2), 139-155.

Cornish, K. (2017). Alternative Natural Rubber Crops: Why Should We Care? *Technology and Innovation*, *18*(4), 245-256. https://doi.org/10.21300/18.4.2017.245

Cornish, K., Bates, G. M., Slutzky, J. L., Meleshchuk, A., Xie, W., Sellers, K., Mathias, R., Boyd, M., Castaneda, R., Wright, M., & Borel, L. (2019). Extractable Protein Levels in Latex Products, and Their Associated Risks, Emphasizing American Dentistry [Article]. *Biology and Medicine*, *11*, 1+. https://link.gale.com/apps/doc/A601325776/HRCA?u=anon~6a07649f&sid=googleScholar&xid=2ed108ce

Cornish, K., Brichta, J., Yu, P., Wood, D., McGlothlin, M., & Martin, J. (2001). Guayule latex provides a solution for the critical demands of the non-allergenic medical products market. *Agro-Food-Industry hi-tech*, *12*.

Cornish, K., & Brichta, J. L. (2002). Trends in new crops and new uses. In J. Janick & A. Whipkey (Eds.), *Trends in new crops and new uses* (pp. xviii, 599 pages). ASHS Press.

Cornish, K., & Lytle, C. D. (1999). Viral impermeability of hypoallergenic, low protein, guayule latex films. *Journal of Biomedical Materials Research*, *47*(3), 434-437. https://doi.org/https://doi.org/10.1002/(SICI)1097-4636(19991205)47:3<434::AID-JBM20>3.0.CO;2-N

Cornish, K., McMahan, C., Xie, W., Williams, J., Nguyen, K., Kostyal, D., & Marsh, D. (2006). ASTM D1076 Category 4 Latex and quantifying Guayule (NRG) and Hevea (NR) latex protein. Proceedings of the International Latex Conference.

Cornish, K., Williams, J., Hall, J. L., & McCoy, R. G., III. (2008). Production and Properties of Yulex® - The Natural Solution to Latex Allergy. *Rubber Chemistry and Technology*, *81*(4), 709-722. https://doi.org/10.5254/1.3548227

Cornish, K., Xie, W., Kostyal, D., Shintani, D., & Hamilton, R. G. (2015). Immunological Analysis of the Alternate Rubber Crop Taraxacum koksaghyz Indicates Multiple Proteins Cross-Reactive with Hevea brasiliensis Latex Allergens. *Biotechnology & Biomaterials*, *5*(4). https://doi.org/10.4172/2155-952X.1000207

de Groot, H., de Jong, N. W., Duijster, E., van Wijk, R. G., Vermeulen, A., van Toorenenbergen, A. W., Geursen, L., & van Joost, T. (1998). Prevalence of natural rubber latex allergy (Type I and Type IV) in laboratory workers in The Netherlands. *Contact Dermatitis*, *38*(3), 159-163. https://doi.org/https://doi.org/10.1111/j.1600-0536.1998.tb05684.x

Drug Overdose Death Rates. Retrieved July 3, 2023 from https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

El-Orbany, M., & Salem, M. R. (2013). Endotracheal Tube Cuff Leaks: Causes, Consequences, and Management. *Anesthesia & Analgesia*, *117*(2), 428-434. https://doi.org/10.1213/ANE.0b013e318292ee21

Elara Brands, Avoid Fake Gloves to Safeguard Your Business. Retrieved August 1, 2023 from https://elarabrands.com/blog/avoid-fake-gloves-to-safeguard-your-business/

Fentanyl DrugFacts. Retrieved July 3, 2023 from https://nida.nih.gov/publications/drugfacts/fentanyl

Fentanyl: Incapacitating Agent. Centers for Disease Control. Retrieved July 3, 2023 from www.cdc.gov/niosh/ershdb/emergencyresponsecard_29750022.html

Field, E. A. (1997). The use of powdered gloves in dental practice: a cause for concern? *Journal of Dentistry*, *25*(3), 209-214. https://doi.org/https://doi.org/10.1016/S0300-5712(96)00013-9

Gao, P., Horvatin, M., Niezgoda, G., Weible, R., & Shaffer, R. (2016). Effect of multiple alcohol-based hand rub applications on the tensile properties of thirteen brands of medical exam nitrile and latex gloves. *Journal of Occupational and Environmental Hygiene*, *13*(12), 905-914. https://doi.org/10.1080/15459624.2016.1191640

Global Disposable Medical Gloves Market Report, 2030. Grand View Research. Retrieved March 1, 2023 from https://www.grandviewresearch.com/industry-analysis/disposable-medical-gloves-market

Global Disposable Medical Gloves Market Report, 2030. Grand View Research. Retrieved February 1, 2023 from https://www.grandviewresearch.com/industry-analysis/disposable-medical-gloves-market

Greenawald, L. A., Hofacre, K. C., & Fisher, E. M. (2020). Fentanyl and carfentanil permeation through commercial disposable gloves. *J Occup Environ Hyg*, *17*(9), 398-407. https://doi.org/10.1080/15459624.2020.1784426

Guerra, N. B., Sant'Ana Pegorin, G., Boratto, M. H., de Barros, N. R., de Oliveira Graeff, C. F., & Herculano, R. D. (2021). Biomedical applications of natural rubber latex from the rubber tree Hevea brasiliensis. *Materials Science and Engineering: C*, *126*, 112126. https://doi.org/https://doi.org/10.1016/j.msec.2021.112126

Hamilton, R. G., & Cornish, K. (2010). Immunogenicity studies of guayule and guayule latex in occupationally exposed workers. *Industrial Crops and Products*, *31*(1), 197-201. https://doi.org/https://doi.org/10.1016/j.indcrop.2009.09.012

Hamilton, V. A., & Grap, M. J. (2012). The role of the endotracheal tube cuff in microaspiration. *Heart Lung*, *41*(2), 167-172. https://doi.org/10.1016/j.hrtlng.2011.09.001

Herkins, A., & Cornish, K. (2023). Durability Variation Among Medical Gloves Made from Existing and New Elastomers Poses a Risk to Public Health. *Global Challenges*, *7*(9). https://doi.org/10.1002/gch2.202300100

Ikeda, Y., Junkong, P., Ohashi, T., Phakkeeree, T., Sakaki, Y., Tohsan, A., Kohjiya, S., & Cornish, K. (2016). Strain-induced crystallization behaviour of natural rubbers from guayule and rubber dandelion revealed by simultaneous time-resolved WAXD/tensile measurements: indispensable function for sustainable resources [10.1039/C6RA22455E]. *RSC Advances*, *6*(98), 95601-95610. https://doi.org/10.1039/C6RA22455E

Johnson, R. L., & Schmidt-Rohr, K. (2014). Quantitative solid-state 13C NMR with signal enhancement by multiple cross polarization. *J Magn Reson*, *239*, 44-49. https://doi.org/10.1016/j.jmr.2013.11.009

Junkong, P., Cornish, K., & Ikeda, Y. (2017). Characteristics of mechanical properties of sulphur cross-linked guayule and dandelion natural rubbers

[10.1039/C7RA08554K]. *RSC Advances*, *7*(80), 50739-50752. https://doi.org/10.1039/C7RA08554K

Junkong, P., Matsushima, Y., Phakkeeree, T., Cornish, K., & Ikeda, Y. (2019). Influence of Strain-Induced Crystallization on Stress Softening of Sulfur Cross-Linked Unfilled Guayule and Dandelion Natural Rubbers. *Rubber Chemistry and Technology*, *92*(2), 388-398. https://doi.org/10.5254/rct.19.81481

Junkong, P., Ohashi, T., Phakkeeree, T., Sakaki, Y., Tohsan, A., Cornish, K., & Ikeda, I. (2017). Comparative Study on Strain Induced Crystallization Behaviours of Sulphur crosslinked Guayule Natural Rubber and Synthetic Isoprene Rubber. *Kautschuk Gummi Kunststoffe*, *8*, 38-43.

King-Smith, N., Molnar, K., Blakeslee, J. J., McMahan, C. M., Pillai, A. S., Mutalkhanov, M., Puskas, J. E., & Cornish, K. (2023). Extractable latex yield from Taraxacum kok-saghyz roots is enhanced by increasing rubber particle buoyancy. *Industrial Crops and Products*, *206*, 117698. https://doi.org/https://doi.org/10.1016/j.indcrop.2023.117698

Lathan, S. R. (2010). Caroline Hampton Halsted: the first to use rubber gloves in the operating room. *Proc (Bayl Univ Med Cent)*, *23*(4), 389-392. https://doi.org/10.1080/08998280.2010.11928658

Li, Z., & Fox, J. M. (2012). Mapping rubber tree growth in mainland Southeast Asia using time-series MODIS 250 m NDVI and statistical data. *Applied Geography*, *32*(2), 420-432. https://doi.org/10.1016/j.apgeog.2011.06.018

Liang, L., Dong, J., & Yue, D. (2019). Branched EHNBR and its properties with enhanced low-temperature performance and oil resistance. *RSC Adv*, *9*(55), 32130-32136. https://doi.org/10.1039/c9ra03656c

Liu, P., Wen, H., Harich, F. K., He, C. H., Wang, L. X., Guo, X. M., Zhao, J. W., Luo, A. D., Yang, H. P., Sun, X., Yu, Y., Zheng, S. B., Guo, J., Li, L., & Zhang, L. (2017). Conflict between conservation and development: cash forest encroachment in Asian elephant distributions. *Scientific Reports*, *7*. https://doi.org/http://doi.org/10.1038/s41598-017-06751-6

Liu, W. J., Hu, H. B., Ma, Y. X., & Li, H. M. (2006). Environmental and socioeconomic impacts of increasing rubber plantations in Menglun township, southwest China. *Mountain Research and Development*, *26*(3), 245-253. https://doi.org/Doi 10.1659/0276-4741(2006)26[245:Easioi]2.0.Co;2

Luckraz, H., Manga, N., Senanayake, E. L., Abdelaziz, M., Gopal, S., Charman, S. C., Giri, R., Oppong, R., & Andronis, L. (2018). Cost of treating ventilator-associated pneumonia post cardiac surgery in the National Health Service: Results from a propensity-matched cohort study. *J Intensive Care Soc*, *19*(2), 94-100. https://doi.org/10.1177/1751143717740804

Malaysian Rubber Board, M. R. C. (2023). *Consumption of rubber worldwide from 2000 to 2022 (in million metric tons)*. Retrieved January 18, 2024 from https://www.statista.com/statistics/618815/total-world-consumption-of-natural-and-synthetic-rubber/

Man-Systems Integration Standards. NASA. https://msis.jsc.nasa.gov/sections/section03.htm

Medical Device Shortages List. U.S. Food and Drug Administration. Retrieved April 11, 2022 from https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/medical-device-shortages-during-covid-19-public-health-emergency

Medical Gloves Market - Global Outlook & Forecast 2022-2027. Research and Markets. Retrieved April 11, 2022 from https://www.researchandmarkets.com/reports/5403544/medical-gloves-market-global-outlook-and?utm_source=BW&%3Butm_medium=PressRelease&%3Butm_code=mbrq64&%3Butm_campaign=1578882%2B-%2BGlobal%2B%2418.56%2BBn%2BMedical%2BGloves%2BMarket%2BOutlook%2B%26%2BForecast%2Bto%2B2026%2Bwith%2BCOVID-19%2BImplication%2BAnalysis&%3Butm_exec=chdo54prd

Meyer, J. D., Chen, Y., Holt, D. L., Beck, M. H., & Cherry, N. M. (2000). Occupational contact dermatitis in the UK: a surveillance report from EPIDERM and OPRA. *Occup Med (Lond)*, *50*(4), 265-273. https://doi.org/10.1093/occmed/50.4.265

Michel, R., & Cornish, K. (2015). *Comparative Durability and Abrasion Resistance of Natural and Synthetic Latex Gloves* International Latex Conference, https://www.rubbernews.com/assets/PDF/RN10078185.PDF

Michel, R., & Cornish, K. (2016). Comparing Natural, Synthetic Latex Gloves. *Rubber & Plastic News*. https://s3-prod.rubbernews.com/s3fs-public/RN10326818.PDF

Mooibroek, H., & Cornish, K. (2000). Alternative sources of natural rubber. *Applied Microbiology and Biotechnology*, *53*(4), 355-365. https://doi.org/DOI 10.1007/s002530051627

Moon, K. M., Donaworth, S., Hagele, M. S., Kim, S. S., Willer, B. L., & Tobias, J. D. (2022). Endotracheal Tube Cuff Pressures in the Operating Room of a Pediatric Hospital: A Quality Improvement Initiative. *Pediatr Qual Saf*, *7*(6), e619. https://doi.org/10.1097/pq9.0000000000000619

Morton, M. (1981). History of Synthetic Rubber. *Journal of Macromolecular Science-Chemistry*, *A 15*(7), 1289-1302. https://doi.org/Doi 10.1080/00222338108056786

Musikavong, C., & Gheewala, S. H. (2017). Assessing ecological footprints of products from the rubber industry and palm oil mills in Thailand. *Journal of Cleaner Production*, *142*, 1148-1157. https://doi.org/10.1016/j.jclepro.2016.08.117

Mylon, P., Lewis, R., Carré, M. J., Martin, N., & Brown, S. (2014). A study of clinicians' views on medical gloves and their effect on manual performance. *Am J Infect Control*, *42*(1), 48-54. https://doi.org/10.1016/j.ajic.2013.07.009

Nair, K. P. (2021). Rubber (Hevea brasiliensis). In K. P. Nair (Ed.), *Tree Crops : Harvesting Cash from the World's Important Cash Crops* (pp. 287-332). Springer International Publishing. https://doi.org/10.1007/978-3-030-62140-7_8

Nakayama, N., Aoki, A., & Hayashi, T. (1994). Carbon-13 NMR chemical shift assignments of poly(vinyl chloride) based on the 2D-INADEQUATE spectrum. *Macromolecules*, *27*(1), 63-68. https://doi.org/10.1021/ma00079a011

Nguyen, K., Williams, J., Wavrin, R., Fishman, B., & Cornish, K. (2007). Guayule (NRG) Yulex® Latex Product Performance. Proceedings of the 10th International Latex Conference, Las Vegas, NV.

Nseir, S., Brisson, H., Marquette, C.-H., Chaud, P., Di Pompeo, C., Diarra, M., & Durocher, A. (2009). Variations in endotracheal cuff pressure in intubated critically ill patients: prevalence and risk factors. *European Journal of Anaesthesiology | EJA*, *26*(3), 229-234. https://doi.org/10.1097/EJA.0b013e3283222b6e

Obrecht, W., Lambert, J.-P., Happ, M., Oppenheimer-Stix, C., Dunn, J., & Krüger, R. Rubber, 4. Emulsion Rubbers. In *Ullmann's Encyclopedia of Industrial Chemistry*. https://doi.org/https://doi.org/10.1002/14356007.o23_o01

Pak, V. M., Watkins, M., & Green-McKenzie, J. (2012). What Is the Role of Thiurams in Allergy to Natural Rubber Latex Products? *Journal of Occupational and Environmental Medicine*, *54*(5), 649-650. https://doi.org/10.1097/JOM.0b013e31824be452

Phalen, R. N., Le, T., & Wong, W. K. (2014). Changes in chemical permeation of disposable latex, nitrile, and vinyl gloves exposed to simulated movement. *J Occup Environ Hyg*, *11*(11), 716-721. https://doi.org/10.1080/15459624.2014.908259

Phommexay, P., Satasook, C., Bates, P., Pearch, M., & Bumrungsri, S. (2011). The impact of rubber plantations on the diversity and activity of understorey insectivorous bats in southern Thailand. *Biodiversity and Conservation*, *20*(7), 1441-1456. https://doi.org/10.1007/s10531-011-0036-x

Rahimi, A., & Mashak, A. (2013). Review on rubbers in medicine: natural, silicone and polyurethane rubbers. *Plastics, Rubber and Composites*, *42*(6), 223-230. https://doi.org/10.1179/1743289811y.0000000063

Ramirez Cadavid, D. A., Layman, R. R., Nishino, T., Slutzky, J. L., Li, Z., & Cornish, K. (2022). Guayule Natural Rubber Latex and Bi2O3 Films for X-ray Attenuating Medical Gloves. *Materials*, *15*(3), 1184. https://www.mdpi.com/1996-1944/15/3/1184

Rego, A., & Roley, L. (1999). In-use barrier integrity of gloves: latex and nitrile superior to vinyl. *Am J Infect Control*, *27*(5), 405-410. https://doi.org/10.1016/s0196-6553(99)70006-4

Roy, D. R. (2000). Latex glove allergy--dilemma for health care workers. An overview. *AAOHN J*, *48*(6), 267-277. https://www.ncbi.nlm.nih.gov/pubmed/11249374

Salehi, M., Bahmankar, M., Naghavi, M. R., & Cornish, K. (2022). Rubber and latex extraction processes for Taraxacum kok-saghyz. *Industrial Crops and Products*, *178*, 114562. https://doi.org/https://doi.org/10.1016/j.indcrop.2022.114562

Samantarai, S., Nag, A., Singh, N., Dash, D., Basak, A., Nando, G. B., & Das, N. C. (2019). Chemical modification of nitrile rubber in the latex stage by functionalizing phosphorylated cardanol prepolymer: A bio-based plasticizer and a renewable resource. *Journal of Elastomers & Plastics*, *51*(2), 99-129. https://doi.org/10.1177/0095244318768644

Sengupta, P., Sessler, D., Maglinger, P., Wells, S., Vogt, A., Durrani, J., & Wadhwa, A. (2004). Endotracheal tube cuff pressure in three hospitals, and the volume required to produce an appropriate cuff pressure. *BMC Anesthesiol*, *4*(8).

Shah, A. A., Hasan, F., Shah, Z., Kanwal, N., & Zeb, S. (2013). Biodegradation of natural and synthetic rubbers: A review. *International Biodeterioration & Biodegradation*, *83*, 145-157. https://doi.org/10.1016/j.ibiod.2013.05.004

Siler, D. J., Cornish, K., & Hamilton, R. G. (1996). Absence of cross-reactivity of IgE antibodies from subjects allergic to Hevea brasiliensis latex with a new source of natural rubber latex from guayule (Parthenium argentatum). *Journal of Allergy and Clinical Immunology*, *98*(5), 895-902. https://doi.org/Doi 10.1016/S0091-6749(96)80005-4

Siler, D. J., Goodrich-Tanrikulu, M., Cornish, K., Stafford, A. E., & McKeon, T. A. (1997). Composition of rubber particles of Hevea brasiliensis, Parthenium argentatum, Ficus elastica, and Euphorbia lactiflua indicates unconventional surface structure. *PLANT PHYSIOLOGY AND BIOCHEMISTRY-PARIS-*, *36*, 881-890.

Soratana, K., Rasutis, D., Azarabadi, H., Eranki, P. L., & Landis, A. E. (2017). Guayule as an alternative source of natural rubber: A comparative life cycle assessment with Hevea and synthetic rubber. *Journal of Cleaner Production*, *159*, 271-280. https://doi.org/10.1016/j.jclepro.2017.05.070

Sudhoff, T. H., Seidl, R. O., Estel, B., & Coordes, A. (2015). Association of Oversized Tracheal Tubes and Cuff Overinsufflation With Postintubation Tracheal Ruptures. *Clin Exp Otorhinolaryngol*, *8*(4), 409-415. https://doi.org/10.3342/ceo.2015.8.4.409

Tan, J. K. S., Song, S. W., Zeng, J., & Lo, C. H. (2023). A hand-targeted auxiliary personal protective equipment for intervention of fomite transmission of viruses. *Bioengineering & Translational Medicine*, *8*(5), e10411. https://doi.org/https://doi.org/10.1002/btm2.10411

Thomas, S., Aldlyami, E., Gupta, S., Reed, M. R., Muller, S. D., & Partington, P. F. (2011). Unsuitability and high perforation rate of latex-free gloves in arthroplasty: a cause for concern. *Arch Orthop Trauma Surg*, *131*(4), 455-458. https://doi.org/10.1007/s00402-010-1146-8

Tlili, M. A., Belgacem, A., Sridi, H., Akouri, M., Aouicha, W., Soussi, S., Dabbebi, F., & Ben Dhiab, M. (2018). Evaluation of surgical glove integrity and factors associated with glove defect. *American Journal of Infection Control*, *46*(1), 30-33. https://doi.org/https://doi.org/10.1016/j.ajic.2017.07.016

van Beilen, J. B., & Poirier, Y. (2007). Guayule and Russian Dandelion as Alternative Sources of Natural Rubber. *Critical Reviews in Biotechnology*, *27*(4), 217-231. https://doi.org/10.1080/07388550701775927

Venkatachalam, P., Geetha, N., Sangeetha, P., & Thulaseedharan, A. (2013). Natural rubber producing plants: An overview. *African Journal of Biotechnology*, *Vol. 12*, 1297-1310. https://doi.org/10.5897/AJBX12.016

Venturini, A., Pancake, M., VanCleave, W., Wan, Y., & Cornish, K. (2022). Invention of a Medical Glove Durability Assessment Device. *Inventions*, *7*(3), 62. https://www.mdpi.com/2411-5134/7/3/62

Virdi, R., Grover, B., & Ghuman, K. (2019). "NITROSAMINE SAFE" THIURAM DISULFIDE. *Rubber Chemistry and Technology*, *92*(1), 90-109. https://doi.org/10.5254/rct.18.82617

Walsh, D. L., Schwerin, M. R., Kisielewski, R. W., Kotz, R. M., Chaput, M. P., Varney, G. W., & To, T. M. (2004). Abrasion resistance of medical glove materials. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, *68B*(1), 81-87. https://doi.org/https://doi.org/10.1002/jbm.b.10055

Willoughby, B. G. (1988). A structural analysis of nitrile rubbers—the 13C resonance technique. *Polymer Testing*, *8*(1), 45-70. https://doi.org/https://doi.org/10.1016/0142-9418(88)90036-0

Wood, D. F., & Cornish, K. (2000). Microstructure of Purified Rubber Particles. *Int J Plant Sci*, *161*(3), 435-445. https://doi.org/10.1086/314269

Wu, J. N., Liu, W. J., & Chen, C. F. (2016). Can intercropping with the world's three major beverage plants help improve the water use of rubber trees? *Journal of Applied Ecology*, *53*(6), 1787-1799. https://doi.org/10.1111/1365-2664.12730

Yoda, R. (1998). Elastomers for biomedical applications. *Journal of Biomaterials Science, Polymer Edition*, *9*(6), 561-626. https://doi.org/10.1163/156856298X00046

Young, P. J., Rollinson, M., Downward, G., & Henderson, S. (1997). Leakage of fluid past the tracheal tube cuff in a benchtop model. *Br J Anaesth*, *78*(5), 557-562. https://doi.org/10.1093/bja/78.5.557

Zak, H. N., Kaste, L. M., Schwarzenberger, K., Barry, M. J., & Galbraith, G. M. P. (2000). Health-care workers and latex allergy. *Archives of Environmental Health*, *55*(5), 336-346. https://doi.org/Doi 10.1080/00039890009604026

Zanella, A., Cressoni, M., Epp, M., Stylianou, M., & Kolobow, T. (2008). A double-layer tracheal tube cuff designed to prevent leakage: a bench-top study. *Intensive Care Medicine*, *34*(6), 1145-1149. https://doi.org/10.1007/s00134-008-1016-9

Zhang, H., & Zhang, G. L. (2005). Landscape-scale soil quality change under different farming systems of a tropical farm in Hainan, China. *Soil Use and Management*, *21*(1), 58-64. https://doi.org/10.1079/Sum2005293

Zhang, H. P., Niemczura, J., Dennis, G., Ravi-Chandar, K., & Marder, M. (2009). Toughening Effect of Strain-Induced Crystallites in Natural Rubber. *Physical Review Letters*, *102*(24), 245503. https://doi.org/10.1103/PhysRevLett.102.245503

Zhang, J. G., & Tao, A. L. (2015). Antigenicity, Immunogenicity, Allergenicity. *Allergy Bioinformatics*, *8*, 175-186. https://doi.org/10.1007/978-94-017-7444-4_11

Zomer, R. J., Trabucco, A., Wang, M. C., Lang, R., Chen, H. F., Metzger, M. J., Smajgl, A., Beckschäfer, P., & Xu, J. C. (2014). Environmental stratification to model climate change impacts on biodiversity and rubber production in Xishuangbanna, Yunnan, China. *Biological Conservation*, *170*, 264-273. https://doi.org/10.1016/j.biocon.2013.11.028